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THE SURGICAL TREATMENT OF PITUITARY ADENOMAS

CHAIRMAN'S ADDRESS

FRANCIS C. GRANT, M.D.

PHILADELPHIA

The surgery of pituitary tumors began in 1906, when Schloffer [1] attacked such a lesion by the endonasal or transphenoidal route. His familiarity with the nasal accessory sinuses led him to select this approach. Subsequently this technic was modified by Kanavel [2] in 1909 and by Halstead [3] and by Hirsch [4] in 1910. In 1912 Cushing [5] further modified the transphenoidal approach in minor details and emphasized its value in the treatment of pituitary adenomas by reporting a large series of cases.

However, the disadvantages of the endonasal route, lack of satisfactory exposure, which handicaps the operator especially if the adenoma is solid, danger of meningitis and the technical difficulties inherent in the procedure, forced the development of an intracranial approach. In 1909 Krause,[6] in 1913 Frazier [7] and in 1920 Heuer [8] described an approach from above through the anterior cranial fossa which, with minor modifications resulting from increasing experience with intracranial conditions, has become the accepted method of attacking any intrasellar or extrasellar tumor.

As early as 1907 the development of the roentgen ray had reached the point where its effect on glandular hypertrophy was recognized. In 1909 Gramegna [9] reported prompt but unmaintained improvement in a middle aged acromegalic woman following irradiation of the sella through the mouth. In 1922 Béclère [10] described a case in which a girl with a pituitary tumor had violent headache, visual disturbance and acromegaly. Thirteen years after roentgen therapy her health was perfect with return of menstruation, improvement in visual acuity and recession of acromegaly. Since that time a number of papers dealing with roentgen therapy of pituitary tumors have appeared, the first large group being detailed by Heinismann and Czerny.[11]

A summary of the literature on roentgen therapy suggests that of the three types of adenoma now recognized the basophil adenoma is the most susceptible to this treatment, next the acidophil and lastly the chromophobe. Furthermore, experience seems to show that cystic adenomas are less responsive to this therapy than solid. Lastly, there seems to be a general agreement that, since a careful check of the visual fields will show promptly whether or not roentgen therapy is effective, this treatment should be instituted prior to surgical intervention.

An adenoma of the pituitary gland produces two groups of symptoms: first, those related to direct effect on the gland itself, the endocrine symptoms, and, second, those resulting from increase in the size of the tumor, headache and visual disturbance. A surgical attack on a pituitary lesion is never indicated until vision is threatened. Roentgen therapy may diminish the size of a pituitary adenoma. The verified adenomas in the series under discussion here have been reviewed to determine whether surgery or roentgen treatment has produced the better end results and furthermore whether, in the presence of loss of visual acuity, reduction in the size of the visual fields and optic atrophy, roentgen therapy is to be preferred to surgery as the first method for relief of symptoms.

When a surgical procedure is suggested in the treatment of a disease, the first consideration is the mortality. In this series forty-four transphenoidal operations have been performed in thirty-seven cases with five deaths, an operative mortality of 11.3 per cent and a case mortality of 13.5 per cent, and 126 transfrontal operations in 106 cases with twelve deaths, an operative mortality of 9.5 per cent and a case mortality of 11.3 per cent. The total series of 143 verified pituitary adenomas has therefore a 10 per cent operative and 11.9 per cent case mortality. Of the 126 remaining cases, eighty-four have been adequately followed for two years or longer. These eighty-four cases have been divided into two groups, those in which operation was not preceded or followed by roentgen therapy and those in which such treatment was administered either before or after operation.

In reviewing the literature on the results of the treatment of pituitary adenomas, the necessity for establishing an accurate method for determining increase or decrease of visual function became at once apparent. In an attempt to rule out vague terms and generalities

Read before the Section on Nervous and Mental Diseases at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. Schloffer, H.: Zur Frage der Operationen an der Hypophysis, Beitr. z. klin. Chir. **1**: 767, 1906.
2. Kanavel, A. B.: The Removal of Tumors of the Pituitary by an Intranasal Route, J. A. M. A. **53**: 704 (Nov. 20) 1909.
3. Halstead, A. E.: The Operative Treatment of Tumors of the Hypophysis, Surg., Gynec. & Obst. **10**: 494, 1910.
4. Hirsch, O.: Ueber Methoden der operativen Behandlung von Hypophysis Tumoren auf Endonasalen, Arch. f. Laryng. u. Rhin. **24**: 129, 1910.
5. Cushing, Harvey: The Pituitary Body and Its Disorders, Philadelphia, J. B. Lippincott Company, 1912.
6. Krause, F.: Freiligung der Hypophysis, Deutsche Klin. **8**: 1004, 1909.
7. Frazier, C. H.: An Approach to the Hypophysis Through the Anterior Cranial Fossa, Ann. Surg. **59**: 145, 1913.
8. Heuer, G. J.: Surgical Experiences with an Intracranial Approach to Chiasmal Lesions, Arch. Surg. **1**: 368 (Sept.) 1920.
9. Gramegna, A.: Un cas d'acromégalie traité par radiothérapie, Rev. neurol. **17**: 15-17, 1909.
10. Béclère, Antoine: Technique, résultats, indications et contre-indications de la roentgenthérapie des tumeurs hypophysaires, Rev. neurol. **39**: 808-816, 1922.
11. Heinismann, J. I., and Czerny, L. I.: Die Röntgen Therapie der Hypophysentumoren, Strahlentherapie **24**: 331-335, 1926.

I decided to adapt the method devised by Snell [12] for determining visual function, which has been accepted as the basis for determining compensation following ocular injuries by many state compensation boards. Briefly this consists in finding the coefficient of function for the visual field and visual acuity in a given case from standard tables. The product of these figures equals the percentage of visual efficiency. In this way a more accurate standard for comparison of gain or loss in vision over a period of years can be obtained between the results of operation, as against operation plus roentgen treatment or roentgen treatment alone in this series of eighty-four adenomas.

TABLE 1.—*Operative Results in 143 Cases*

17 deaths	10% operative	11.9% case	
Transphenoidal route			37 cases
44 operations			5 deaths
Mortality	Operative 11.3%	Case	13.5%
Transfrontal route			106 cases
Mortality	Operative 10%	Case	11.9%

Among these eighty-four patients thirty-eight were subjected to one or more operations and forty-six received roentgen treatment in addition to a surgical procedure.

In the group of thirty-eight on whom operation alone was performed, seven were operated on by the transphenoidal route, four acidophil and three chromophobe tumors, and thirty-one by the transfrontal approach, twenty-seven chromophobe and four mixed adenomas. In twenty-one of these cases the results were considered to be good. Beginning with an average visual efficiency of 35 per cent following operation, this was increased to 66 per cent over a period averaging 7.2 years. Two of this group have been followed for only three years and three for more than ten years. In seventeen cases a poor result followed surgical intervention. Beginning with an average visual efficiency of 32 per cent by the end of an average 7.2 years after operation, the average efficiency was 23 per cent. Five of these patients had a transphenoidal procedure, three acidophil and two chromophobe adenomas. The twelve transfrontal operations verified nine chromophobe and three mixed adenomas.

TABLE 2.—*Results of Surgical Operation*

Good Results	
21 cases pre-operative visual efficiency	35%
Postoperative visual efficiency	66%
Average follow-up	7.2 years
Poor Results	
17 cases pre-operative visual efficiency	32%
Postoperative visual efficiency	25%
38 cases. Average follow-up	7.2 years

Forty-six patients were operated on and also received roentgen therapy. Thirty-two fall into a satisfactory result group, having been followed for an average of seven years after treatment and showing an average increase in visual efficiency from 24.7 per cent to 60.5 per cent. Of these adenomas, fourteen were cystic and eighteen were solid. A transphenoidal operation was carried out in six instances on five acidophil and a single chromophobe adenoma. The transfrontal attack in twenty-six cases verified twenty chromophobe and six mixed adenomas. In fourteen cases the results following operation plus roentgen therapy were unsatisfactory. These cases were followed for an average of nine years and the visual efficiency fell from an average of 50.4 per cent after treatment to 36.5 per cent. Eight adenomas were cystic, six solid. In eight instances the transfrontal approach was carried through, verifying a chromophobe adenoma. In six cases a transphenoidal attack was used, revealing an acidophil tumor in four and a chromophobe in two instances.

Through the courtesy of the Roentgen Ray Department at the Hospital of the University of Pennsylvania, I have had access to the records of ten patients treated by roentgen rays alone and followed for an average of 3.7 years. While no tumor from any of these patients has been verified histologically the sella turcica was enlarged in eight instances, five clinical acidophil and three chromophobe tumors, with temporal field cuts on one or both sides and optic atrophy. Two patients had indications suggesting a basophilic adenoma. The average visual efficiency was 68.9 per cent and increased to 87.1 per cent after roentgen treatment.

The details of the roentgen treatment which these patients received are as follows: Five fields are used, two temporal, two occipital and one bregmatic. Each field is 12 cm. in diameter. At a distance of 50 cm. with a voltage of 200 kilovolts, a milliamperage of 20, an effective wavelength of 0.17 angstrom, a roentgen output of 43 per minute and two filters used, one of copper 0.5 mm. and one of aluminum 1 mm. in thickness, 1,600 roentgens is given over each field at a rate of 300 roentgens a day. Thus in three or four weeks a dose of about 3,200 roentgens reaches the tumor. If necessary this dose is repeated at the end of three months.

TABLE 3.—*Results of Surgical Operation Plus Roentgen Therapy*

Good Results	
32 cases pretreated visual efficiency	24.7%
After treated visual efficiency	60.5%
Average follow-up	7 years
Poor Results	
14 cases pretreated visual efficiency	50.4%
After treated visual efficiency	36.5%
46 cases. Average follow-up	9 years

A review of the literature seems to indicate that about 25 per cent of pituitary adenomas are cystic, the remainder being solid. Of these 143 cases, sixty-two, or 43 per cent, were cystic. The criterion on which I have based the consistency of the tumor has been the operative notes. If the operator stated that at the time the capsule of the tumor was incised the contents flowed out with prompt or slow collapse of the mass, I have considered the adenoma to be cystic. If, however, after slitting the capsule the wound simply gaped open without spontaneous escape of the enclosed tissue and without reduction in its size, such an adenoma has been classed as solid.

My impression has always been that cystic tumors, because of their prompt collapse following incision of the capsule, gave the best and most immediate results in recovery of vision and enlargement of the fields. In a review of the twenty-one cases classed as "good results following surgery," this impression is sustained, for six of these tumors were solid and fifteen cystic. Furthermore, in the group of seventeen patients designated as having had fair results following surgery in twelve the tumor was solid and in five cystic.

12. Snell, A. C.: An Analysis of the Compensation Problem as It Relates to Ocular Injury, Arch. Ophthl. **53**: 37 (Jan.) 1924.

Henderson,[13] Schnitker,[14] Dyke and Hare [15] and Rand and Taylor [16] have all stated that cystic adenomas are more roentgen resistant than solid. Of the thirty-two adenomas listed as showing good results following operation and roentgen treatment, fourteen were cystic and eighteen solid. In the group of fourteen adenomas classed as unsatisfactory following operation plus roentgen therapy eight were cystic and six solid. However, in results of the combined treatment the value of roentgen therapy is hard to differentiate from that of the operation because of its administration before the patient's discharge from the hospital. Prior to three years ago I expected major results in visual improvement from operation and advised irradiation simply with the hope of prolonging this improvement.

TABLE 4.—*Results of Roentgen Treatment Alone*

10 Cases	
Pretreated visual efficiency	68.9%
Posttreated visual efficiency	87.1%
Average follow-up	3.7 years

A comparison of the thirty-eight cases treated by surgery alone with the forty-six in which the combined therapy was employed shows definitely that roentgen treatment is valuable. Twenty-one of thirty-eight cases, or 55 per cent, showed marked improvement following surgery alone. But the combined treatment produced marked improvement in thirty-two of forty-six, or 70 per cent. Again the increase in visual acuity averaged from 35 to 66 per cent following surgery and from 24 to 60 per cent when roentgen therapy was added.

Based on a review of the cases, I believe that, although it is impossible to determine prior to operation whether a pituitary adenoma is solid or cystic, roentgen exposure is indicated as a primary therapeutic measure. Only occasionally does it produce untoward results. In my experience three patients have become unconscious following irradiation, two dying in coma. In one case at least the fatality was due to hemorrhage into the tumor. All three patients were old "burned out" pituitary sufferers with advanced evidence of glandular hypofunction. Headache, nausea and epilation are unimportant consequences of this treatment.

In my opinion roentgen treatment does not render subsequent surgical intervention more difficult by causing adhesions or in other ways. I cannot supply figures showing its effect on operative mortality. I do, however, feel very strongly that roentgen treatment often lulls the patient into an unjustified feeling of security. Of eleven patients who had transfrontal craniotomies, roentgen treatment had checked or even slightly improved the visual efficiency. Operative treatment had therefore been postponed for from seven to twenty-eight months. When further loss of vision occurred and operative intervention was necessary, in eight the adenoma had broken through its capsule and overflowed the sella into the cranial cavity. Five operative deaths occurred in this group alone. Therefore, unless roentgen therapy produces within six weeks of the beginning of treatment a marked improvement in the visual fields and visual acuity, surgery is indicated. That irradiation simply prevents further loss of vision and holds it stationary for a time is not enough. When again visual deterioration occurs, the surgeon may be confronted by a large spreading tumor—a hopeless situation from the surgical point of view with a high mortality rate. The patient has been allowed to drift past the optimal time for surgical intervention because of an apparent check in the progression of symptoms by roentgen therapy. Therefore I feel that whether irradiation is used preoperatively, postoperatively as a prophylactic measure or after the operative improvement has commenced to recede in an attempt to cause further shrinkage in the size of the adenoma, its use should be continued only if actual improvement can be shown by repeated and careful visual tests.

Of fifteen cases in which the records are available, marked evidence of improvement in vision and the perimetric tests was apparent after three weeks in nine. Four of these patients had acidophilic and five chromophobe adenomas. Among the other six cases, three could not be followed and three came to operation on an average of twelve months after the last roentgen treatment. Two patients had large spreading tumors that had escaped from the sella. One died following surgical intervention; the second was unimproved. The third patient had a cystic adenoma which was easily collapsed. However, visual efficiency had been reduced to 21 per cent and increased to 28 per cent following operation. The delayed improvement consequent on roentgen therapy described by Towne [17] and appearing only after six months or a year has not been seen in this series. If roentgen therapy is effective, improvement should appear within six weeks of the commencement of a vigorous course of such treatment.

Complete surgical removal of an adenoma is usually impossible. The vessels forming the circle of Willis surround the sella, are often adherent to the capsule of the adenoma and may be torn if too radical an attempt at removal is attempted. The hypothalamic region above and behind the tumor may be injured during manipulation or retraction with consequent and often fatal hyperthermia. The safest surgical attack on an adenoma is an intracapsular enucleation with sufficient reduction in the size of the tumor to relieve pressure on the optic nerves and removal of all easily accessible capsule. Roentgen therapy should then be relied on to prevent recurrence. My experience suggests that this treatment should be given within six weeks of the original operation. Every such patient should have visual field studies carried out repeatedly at three month intervals thereafter. In this way evidence of recurrence is promptly recognized and can be properly dealt with before the adenoma becomes too large.

TABLE 5.—*Surgery vs. Surgery Plus Roentgen Therapy*

Surgery alone	38 cases
Marked improvement	21 cases or 55 %
Increase in visual efficiency	35% to 66%
Surgery plus roentgen therapy	46 cases
Marked improvement	32 cases or 70%
Increase in visual efficiency	24% to 60%

The effect of roentgen treatment is beneficial in a sufficiently high percentage of pituitary adenomas to warrant its use preoperatively. In visual field studies an accurate and easily verified control of the results of

13. Henderson, W. R.: The Pituitary Adenomata, Brit. J. Surg. **26:** 811-921 (April) 1939.

14. Schnitker, M. T.; Cutler, E. C.; Bailey, O. T., and Vaughan, W. W.: The Chromophobe Adenomas of the Pituitary, Am. J. Roentgenol. **40:** 645-659 (Nov.) 1938.

15. Dyke, C. C., and Hare, C. C.: Roentgen Therapy of Pituitary Tumors, Proceedings of the Society for Research in Nervous and Mental Disease, Baltimore, Williams & Wilkins Company, 1938, pp. 651-663.

16. Rand, C. W., and Taylor, R. G.: Irradiation in Tumors of Pituitary Gland, Arch. Surg. **30:** 103-150 (Jan.) 1935.

17. Towne, E. B.: Treatment of Pituitary Tumors: Role of Roentgen Ray and Surgery Therein, Ann. Surg. **91:** 29-36 (Jan.) 1930.

roentgen therapy is available. Three weeks' treatment as outlined should be administered with a careful perimetric field examination at the end of that period. Only if the visual acuity and fields are unimproved at the end of that period is surgical intervention justified. Postoperatively roentgen treatment seems definitely to prolong the period before evidence of recurrence of the adenoma appears.

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THE ROENTGEN THERAPY OF PITUITARY ADENOMAS

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As physicians specializing in nervous and mental diseases, we have all known of the increasingly good results following surgical attack on the pituitary adenomas, results which have been steadily improving for the past twenty-five years. We have heard again this afternoon [1] of the magnificent work which is being done by the neurosurgeon. I have no quarrel with surgeons but only admiration for their courage as well as their technical skill and for their low mortality, which, in the last ten years of Dr. Cushing's series,[2] reached the astonishing figure of only 2.4 per cent. (The mortality is not as low in the majority of neurosurgical clinics, being probably nearer 10 per cent.) Recently an accurate, complete and detailed report of a follow-up study of Cushing's 338 cases of pituitary adenoma by Henderson [3] stated that the good results following surgical procedure can be prolonged and some of the recurrences prevented by postoperative roentgen therapy.

Chromophobe Adenomas: The Percentage of Patients Without Recurrence at Five Years, According to the Type of Operation and X-Ray Treatment [4]

Treatment	No. of Cases	Cases Without Recurrence at 5 Yr.	
		No.	Percentage
Transphenoidal operation only	67	22	32.8
Transfrontal operation only	40	23	57.5
Transphenoidal operation plus roentgen therapy	49	32	65.3
Transfrontal operation plus roentgen therapy	31	27	87.1

If surgical therapy produces good immediate results and surgical therapy plus irradiation extends and prolongs those results, what can be expected from irradiation alone without surgical treatment? There are three important fundamental principles to be established before consideration of the results of roentgen therapy alone:

1. A survival period of three, five or even ten years is no criterion of results as it is in outspoken malignant conditions such as osteogenic sarcomas or uterine carcinomas. We must judge our results by the patient's restoration to health, a return to a normal mode of living and, particularly in the chromophobe type of adenoma, by restoration of vision. On the whole, the degree of improvement in vision and the duration of that improvement are the best guides as to effective therapy. It is worthy of note here that failing vision was the chief complaint of 87.5 per cent of Cushing's 260 patients with verified chromophobe adenomas.

2. Nearly all the patients irradiated in Cushing's series, as reported by Henderson, were treated with relatively low voltage and small doses, and yet some extremely good results were recorded. One would now consider those patients as being definitely undertreated. With the modern accurate penetrating radiation one can and does give larger and more accurately measured total doses, spreading treatment over a longer period and using more portals.[5] One can justifiably expect from present indications a greater effect on the tumor.

3. Pituitary adenomas are extremely variable in their rate of growth, their direction of growth, or extension, and their effect on health and vision. Like all adenomas of endocrine glands, they are even liable to spontaneous remissions, and one must keep this possibility in mind when evaluating results. It might be more valuable to analyze and compare failures rather than to consider only good results.

As sample cases, illustrating the wide variation in the symptoms, signs and results of treatment, I present in brief the histories of three patients:

REPORT OF CASES

CASE 1.—A man aged 47 years had had headaches for eight years, ease of fatigue for five years, failing vision for two years and a recent gain in weight. The visual fields showed large central scotomas and inferior quadrantal defects (Henderson's group 4). Visual acuity was 20/30 —2 in the right eye and 20/200 in the left. The basal metabolic rate was —37 per cent. Roentgenograms revealed an enlarged pituitary fossa 25 by 14 mm. in size, with partial destruction of the posterior clinoids and dorsum sellae but no general signs of increased intracranial pressure. Roentgen therapy was begun Aug. 3, 1935, three portals being used in rotation (both temporal areas and one midline supra-orbital area), with daily doses of 300 roentgens to one portal. The total number of treatments was nine (three to each portal), and the total dose was three times 900 roentgens in ten days. Objective improvement in the visual fields and in visual acuity was demonstrable by August 12, the day of the ninth treatment, and improvement continued after the cessation of treatment. The visual fields and the visual acuity had returned to normal at examination in February 1936, and they have remained normal to date (May 1939), almost four years. This response was unusually prompt but highly satisfactory, particularly in this patient, who is the brother of one of our house physicians. Physicians all know how members of their families are prone to develop complications and unusual reactions in response to standard therapy.

CASE 2.—This patient is quite a contrast to the first. Both his history and results of his physical examination were atypical, with the roentgenographic appearance of his sella contributing largely to the diagnosis. He was a retired bank teller aged 54, who for nine years had suffered petit mal convulsions and for three years grand mal attacks with failing memory, gain in weight, loss of libido and failing vision. Examination revealed slight right exophthalmos, bilateral primary optic atrophy with left upper homonymous quadrantanopia, partial anosmia, nerve deafness on the left and a basal metabolic rate of —23 per cent. These features were hardly suggestive of a pituitary adenoma, but the roentgenograms revealed marked destruction of the sella and of the adjacent sphenoid bone with an extension of the destructive process downward, backward and to the left,

Read before the Section on Nervous and Mental Diseases at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. Grant, Francis C.: The Surgical Treatment of Pituitary Adenomas, this issue, p. 1279.

2. Cushing, Harvey: Intracranial Tumours; Notes upon a Series of Two Thousand Verified Cases with Surgical-Mortality Percentages Pertaining Thereto, Springfield, Ill., Charles C. Thomas, 1932.

3. Henderson, W. R.: The Pituitary Adenomata: A Follow Up Study of the Surgical Results in 338 Cases, Brit. J. Surg. **26**: 811 (April) 1939.

4. Henderson,[3] p. 865.

5. Schnitker, Max T.; Cutler, Elliott C.; Bailey, Orville T., and Vaughan, Walter W.: The Chromophobe Adenomas of the Pituitary, Am. J. Roentgenol. **40**: 645 (Nov.) 1938.

where there was erosion of the tip of the petrous ridge. The observations could best be explained by a large pituitary adenoma, with invasion and destruction of the base of the skull and extension into the left temporal lobe causing the homonymous quadrantanopia and extension into the cerebellopontile angle causing the deafness on the left.

Roentgen therapy was instituted in January 1935, with rather mild doses of 300 roentgens a day to the temporal areas, treated alternately, until 600 roentgens had been given to each side. This dose was repeated in March, June and September of that year. There was definite improvement in that the grand mal attacks ceased, but the petit mal seizures continued although they decreased in frequency. With the idea that these seizures might be due to hypoglycemic reactions as reported by Wilder,[6] the patient's blood sugar curve was investigated; it was found to be normal, and injections of insulin did not provoke an attack. The patient's visual fields, however, which are the best index of shrinkage of the tumor, improved only slightly during the irradiation and relapsed to their former state three months after the last treatment. For that reason surgical therapy was offered and accepted; on March 4, 1936, a large amount of tumor tissue was removed through a right transfrontal approach. The patient did not do well after his operation, and he succumbed two days later. At autopsy a huge tumor, 7 by 7 by 4 cm. in size, was found in the sellar region, surrounding the basal arteries and nerves, extending into both temporal fossae, more on the left, and projecting backward, compressing the pons and partly eroding the left petrous tip. Histologically it was a chromophobe adenoma of the pituitary gland. The sella was completely destroyed and the sphenoid sinuses were obliterated by the tumor. This patient may well be chosen to represent some of the failures in either irradiation or surgical treatment of pituitary adenomas. It was obviously impossible to remove more than an inconsequential portion of the tumor surgically and equally impossible to cause adequate shrinkage of the tumor by irradiation. The patient had allowed the tumor to progress to such a size that a satisfactory alleviation of symptoms was impossible by any means.

CASE 3.—This is more typical of what one can ordinarily expect, both clinically and as a result of roentgen therapy. This 30 year old Jewish WPA worker, who was first seen Feb. 14, 1934, complained of having had impotence for four years, blurred vision for three years, gain in weight and discomfort in cold weather for two years and frontal headaches for one year. Roentgenograms of his skull revealed an expanded sella measuring 24 by 30 mm. Physical examination showed adiposity of female distribution, a scanty beard requiring shaving but once a week, a pale dry skin, bitemporal hemianopia, and a basal metabolic rate of —30 per cent. Roentgen treatments totaling 600 roentgens to each temporal portal were given in February, April, September and November 1934. The first improvement in the visual fields was noted at seven months, no improvement having been apparent at five months. The right visual field was normal at eleven months, but there remains a permanent defect in the left lower temporal quadrant, similar to the defects often remaining after operation and interpreted by Henderson and Cushing as being due to counter pressure on the optic nerve by the margin of the optic foramen or the anterior cerebral artery.[7] There has been no recurrence of visual failure to date (May 1939), over five years since irradiation was begun. Potency has returned intermittently and temporarily, but potency is not a reliable index of the efficacy of therapy, as it is affected by too many factors, local and constitutional as well as psychic. I mention it here only because it was the patient's chief complaint, of more importance to him apparently than his failing vision. The patient is otherwise in good condition, his headaches have disappeared and he has more vigor and endurance, but his basal metabolic rate remains low and he shaves but twice a week. No irradiation has been given since 1935.

My results with the chromophobe type of adenoma, with use of roentgen therapy only, are as follows: Fourteen patients were treated; two subsequently were operated on (one as described in the report of case 2). The condition of four patients was hopeless from the start, owing to extensive invasion or intracranial extension (three were dead in three months). Ten cases were suitable for analysis or results, but in two of them therapy was too recent (under two years since first treatment) for evaluation at this time.

Seven of the remaining eight patients (87.5 per cent) have received marked benefits from their irradiations, both as to restoration of vision and as to return of the patient to normal living. Objectively demonstrable improvement in vision of one patient began by the ninth day of treatment (case 1) and of others at various periods up to seven months (case 3). Towne[8] reported at the Eighty-Ninth Annual Session of the American Medical Association that objectively demonstrable improvement in the visual fields might be delayed for a year or even more after commencement of irradiation. The duration of improvement in my cases has lasted from three to five years, with no recurrences so far.

1. Failures, then, occur in the patients with advanced extensive lesions, either invasive in bone or with large intracranial extensions, the group who account for the bulk of Dr. Cushing's postoperative fatalities. (Two patients with borderline tumors which were incompletely removed surgically and then irradiated are still alive, working, and about 90 per cent efficient; they are not included in this group.) 2. Failures may also occur in the cases in which the tumor has been pressing on the optic nerves or chiasm so long that it has produced atrophy of the fibers. This is the same group for which Henderson reported failures after the surgical removal of the adenoma, even with postoperative irradiation. One of my cases fell into this group. Irradiation failed to relieve the defective vision, which the patient had noted for three years. An unusually satisfactory removal of the tumor two months later also failed to improve the visual fields. 3. Cystic tumors, which formed 17 per cent of Cushing's 260 chromophobe tumors, are said not to respond to irradiation. As far as I know, there were no examples in my small series. All but one of the tumors which failed to improve have been examined histologically either at subsequent operation or at autopsy. Henderson noted that even with cystic tumors the recurrences were avoided or delayed by postoperative irradiation, and he urged such treatment in all cases.

The dangers from or following irradiation must be considered. They are real but infrequent. Henderson noted that no late ill effects from roentgen therapy were found in Cushing's series. He did state that in one case extensive adhesions between the adenoma and the chiasm, which prevented a satisfactory surgical removal, were assumed to be due to extensive irradiation elsewhere for more than a year before operation. Henderson also reported that in no case was cystic tumor found after preoperative irradiation, but I have seen an acute hemorrhagic cyst develop after a fairly heavy single roentgen treatment for recurrence after operation. The patient went into coma in a few hours but was relieved by an immediate emergency operation. In Henderson's report, one case of bilateral cataract formation in a young person was attributed to heavy (and perhaps careless) preoperative irradiation. This is a definite possibility, as I have seen it occur under

6. Wilder, Russell M.: Spontaneous Hypoglycemia, Internat. Clin. 3: 143 (Sept.) 1936.
7. Henderson,[3] p. 856.
8. Towne, E. B.: Personal communication to the author.

treatment for other cranial conditions. Edema of the brain is often held up as a possibility, but in all the hundreds of patients I have irradiated for all sorts of cranial or intracranial conditions, I have yet to see a patient with postirradiation edema of the brain. Experiments lead one to believe that the nervous tissue of adults will stand a dosage up to 6,000 roentgens in any one area. One should keep below this dose, therefore, to avoid injury to the vessels and subsequent fibrosis, gliosis or necrosis. Henderson's opinion is that the real and greatest danger in irradiation without operation is the period of delay necessary to determine the results; i. e., while roentgen therapy is being tried, the failure promptly to remove the pressure on the optic chiasm may possibly result, with unsatisfactory responses, in a change from temporary relievable blindness to permanent optic atrophy due to degeneration of the nerve fibers. This question can be answered only by experience over many years and with a much larger series of cases than I am able to report at present. So far I have not seen any patient get worse during or immediately after irradiation, with the exception of the patient with cystic degeneration already mentioned.

A word about the acidophil tumors and acromegaly and their response to irradiation must be included for comparison. Almost everybody agrees that they respond more readily to irradiation than the chromophobe type, that the majority of them can best be treated by irradiation, particularly if there are no field defects (which are rare), and that they are much more liable to spontaneous remissions and waves of activity and inactivity. These tumors grow so slowly in the majority of cases that the eventual result is in doubt for many years. The most distressing symptom of nearly all the patients irradiated was headache, and this was definitely improved or entirely relieved in 90 per cent of the twenty-eight cases. Vaughan has reported our results in detail.[9]

We believe from the results in our cases that acromegaly (and gigantism in adolescents) can be stopped by reasonable doses of roentgen therapy; that the chief symptom, headache, can be relieved in 90 per cent of the cases, and that visual failure due to pressure of an expanding adenoma may also be relieved. Many of the patients with acidophil adenoma, however, go over into a stage of hypopituitarism spontaneously, and this cannot be prevented by roentgen therapy; in fact, it may be hastened by heavy irradiation. It is conceivable, however, that if beginning acromegaly is recognized early enough the hyperactive tumor can be stopped by irradiation, which allows the remaining normal portion of the gland to continue its normal function. Only time and many carefully studied and accurately followed patients can give the answer to that hypothesis.

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ABSTRACT OF DISCUSSION

DR. GEORGE W. CHAMBERLIN, Philadelphia: Our ideas concerning the treatment of pituitary adenoma are changing. Until a few years ago, clinicians regarded these tumors as radioresistant. This feeling arose in part from lack of suitable therapy equipment, which we now possess, and in part from our lack of experience in treating these tumors. Whatever the cause, there is now adequate evidence that roentgen therapy is valuable in the treatment of adenomas of the pituitary. According to statistics presented by Dr. Henderson in his review of 338 cases of pituitary adenoma from Dr. Harvey Cushing's series, about 30 per cent more patients remain well for five years if given roentgen therapy plus operation than remain well after operation alone. That is, 57.5 per cent of the patients who received transfrontal operation only were without recurrence for five years, whereas 87.1 per cent of those who received the same type of operation plus roentgen therapy remained free from recurrence for five years. Dr. Sosman has shown that those patients who have large tumors with extrasellar extensions give a poor prognosis by any method of treatment. Since these lesions are apt to surround fixed structures such as the carotid artery and thus make their surgical treatment hazardous or impossible, it seems reasonable to use roentgen therapy as the procedure of choice. For with the latter method, the result is dependent on cell sensitivity rather than on the size of tumor. I do not believe that preoperative irradiation, properly given, will produce changes in the tissue which make subsequent operation more difficult. The basis for this opinion is the experimental work of Dr. Pendergrass on the effect of radium on the normal tissues of the brain of dogs and also our clinical and pathologic experience in the treatment of brain tumors as reported by Dr. Alpers and Dr. Pancoast in 1933 and by Dr. Frazier, Dr. Alpers and myself in 1937. I believe that Dr. Grant will support this statement on the basis of his surgical observation of these tumors after irradiation. Another group of patients are those with very small tumors as evidenced by slight changes in the visual fields or a sella turcica of top normal size. Here again, in this relatively small group of cases, the technical difficulties encountered by the surgeon in finding the adenoma is sufficient reason for considering treatment by radiation therapy. It is my feeling that the larger group of patients comprising those who have a ballooned-out sella without extrasellar extension but with definite field defects and diminished visual acuity should also receive preoperative irradiation unless there is evidence of a rapid diminution in visual efficiency.

DR. ERNEST SACHS, St. Louis: I came here originally to agree with everything that Dr. Sosman had to say. I read his paper, which he was kind enough to send to me, but in the abstract in the program I read this sentence: "These results justify the conclusion that one should try irradiation in all cases of pituitary adenoma before resorting to surgical intervention," and that is the opinion that was also expressed by Dr. Grant. I must take exception to that opinion and for this reason: I think the clinician or the surgeon has to be guided by the amount of loss of vision that the patient has when he presents himself. A patient now in the hospital is unable with his right eye to read the biggest letters at a distance of 15 feet and in his left eye he has 15/200 vision. He is a farmer. He cannot see well enough even to plant corn in a straight line. To subject that man to a preliminary course of roentgen treatment I consider would be unwise in spite of the fact that there is an operative risk which we cannot deny. I believe that the most important thing to decide in each case is how much visual loss the patient has when he presents himself. If he has an adequate amount of vision and it seems comparatively safe to try high voltage therapy for a short period (I agree with Dr. Grant that it ought not to be tried for more than four or six weeks, anyway), I think it is all right to try roentgen treatment before operation; but if the vision is very seriously impaired I think it is a different story. Regarding the roentgen treatment after operation, I agree with Dr. Sosman that we should give high voltage therapy after the patient has been operated on with the idea of preventing a recurrence, but in my experience that does not always follow. I have in mind a patient who was operated on for the first time six years ago for a pituitary tumor with complete restoration of vision, and he did not receive high voltage roentgen therapy at that time. He was completely relieved for four years and then he returned with a recurrence, and he was then reoperated on and received roentgen therapy after the operation. He had his third recurrence this year and was reoperated on in spite of the fact that he had been given very considerable doses of x-rays by Dr. Moore of our x-ray department. How long he is going to be

9. Vaughan, Walter W.: The Place of Irradiation in Acromegaly, Am. J. Roentgenol. **40**: 660 (Nov.) 1938.

free from his symptoms I do not know. On the other hand, if we see a patient who has a slight loss of vision, I certainly think we ought to give him roentgen treatment.

DR. MERRILL C. SOSMAN, Boston: I feel that I have gotten off lightly as regards the suggestion that I made in the abstract (which I made on purpose) that all patients be treated with roentgen rays first. If you will read the report that Dr. Henderson made, you will find that patients were classified according to the visual difficulty on admission, and that with certain types of visual difficulty, particularly when one eye is blind and the other has a hemianopia, the prospects of good recovery of vision are very poor. So that in the advanced cases that Dr. Sachs mentioned I think the prospects are bad by either or both methods of treatment in the majority of cases as shown in the analysis of a large number of similar groups of patients. In my experience it is not the degree of visual difficulty which is important but the duration over which that visual failure has lasted; and, if visual failure has been present over the period of a year, the chances again are poor either by surgery or by roentgen therapy. I still feel, because of the operative mortality, which averages about 10 per cent, that it is reasonable to try roentgen irradiation when the patient first presents himself and the diagnosis is made.

THE MANAGEMENT OF PATIENTS WITH DIFFUSE PERITONITIS

CAUSED BY PERFORATION OF THE APPENDIX

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In February 1935 we made a statistical and critical analysis of forty-four cases of diffuse peritonitis following perforation of the appendix treated at the Buffalo General Hospital and Buffalo Children's Hospital. In this series of cases there were twenty deaths, or a mortality rate of 45.4 per cent, in two institutions which represented a cross section of the average hospital in this country.

In addition, we obtained the following information: Ninety-seven per cent of the patients were operated on by six different surgeons, and no uniformity of treatment existed. We believe that, omitting surgical judgment, which is a personal and individual equation that cannot be evaluated, the chief means available to combat peritonitis is the intelligent use of morphine, fluids, duodenal decompression and transfusion. The various surgeons used one or two of these agents to the total exclusion of the remainder, and there was no unanimity of opinion as to the indications for their use.

For the sake of clarity we would emphasize the fact that this discussion is limited to diffuse peritonitis and does not include the other complications following perforation of the appendix.

To reduce this mortality rate of 45 per cent, it was obvious that we first had to know, if possible, why patients with diffuse peritonitis die. At postmortem examination these patients presented the following anatomic changes rather consistently: (1) tremendous distention of the entire gastrointestinal tract, (2) high elevation of the diaphragm, (3) compression atelectasis of the lungs above the diaphragm, (4) terminal pneumonia, (5) marked stagnation of blood in the splanchnic and mesenteric vessels, (6) contraction of the spleen and (7) paleness and anemia of the liver.

We feel that these observations point to the fact that such patients die primarily for two reasons: shock and intestinal obstruction.

Keeping these anatomic manifestations in mind and realizing the alterations in physiology that they produce, one finds it possible to correlate them with the clinical picture.

The patient with diffuse peritonitis entering the fourth or fifth day of the illness has a cyanotic hue of the lips and finger nails, falling blood pressure and increased respiratory rate which are manifestations of the large amount of blood stagnated in the splanchnic and mesenteric vessels and not available for the peripheral circulation. The rise in the pulse rate is a compensatory effort of the heart to bring the blood, which it is receiving in a markedly diminished amount, to the tissues of the body.

The high elevation of the diaphragm and associated compression atelectasis are probably the chief factors in the production of the terminal pneumonia. As there is no evidence of primary disease of the kidneys at autopsy, the changes in the urine and blood are the result of dehydration.

With the background that we have constructed, let us now analyze each of the four therapeutic procedures mentioned, namely duodenal decompression, administration of fluids, adequate and intelligent use of morphine, and transfusion, and see what we accomplish in their use and attempt to arrive at concrete indications for employing them.

By means of continuous duodenal decompression as devised by Wangensteen [1] we attempt to alleviate distention by removing gas and fluid from the stomach and intestine and overcome to some extent the high elevation of the diaphragm, with the consequent compression atelectasis of the overlying lungs, and thus remove a factor in the production of a terminal pneumonia. In addition, if we admit that an intestinal obstruction exists in every case, even though paralytic and not mechanical, we are to some extent combating the effects of a high intestinal obstruction.

TABLE 1.—*Diffuse Peritonitis, 1929-1934*

Cases	Deaths	Mortality, Percentage
44	20	45.4

Average time, onset to hospitalization, 72 hours

In using duodenal decompression one must remember that the advance of the tube through the pylorus depends chiefly on the peristaltic action of the stomach. If, therefore, one delays introducing the tube until gastric peristalsis is lost because of the infection and subsequent distention, there can be little hope of the tube entering the duodenum and consequently there will be no real decompression of the small intestine. Another factor is that nausea and emesis vary with different individuals, and these symptoms should not be used as

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Cooperation and aid were given by Drs. K. L. Terplan, Ernst Witebsky, R. S. Hubbard, N. C. Klendshoj and Erwin Neter.

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1. Wangensteen, Owen H.: The Therapeutic Problem in Bowel Obstruction, Springfield, Ill., Charles C. Thomas, Publisher, 1937.

an indication for beginning decompression. To illustrate: It has been our experience that one patient may complain of nausea and emesis with only 500 cc. in his stomach and that another may tolerate 2,000 cc. with no complaints, the latter statement having been proved at autopsy.

In discussing the parenteral administration of fluids one must consider the manifestations of dehydration and

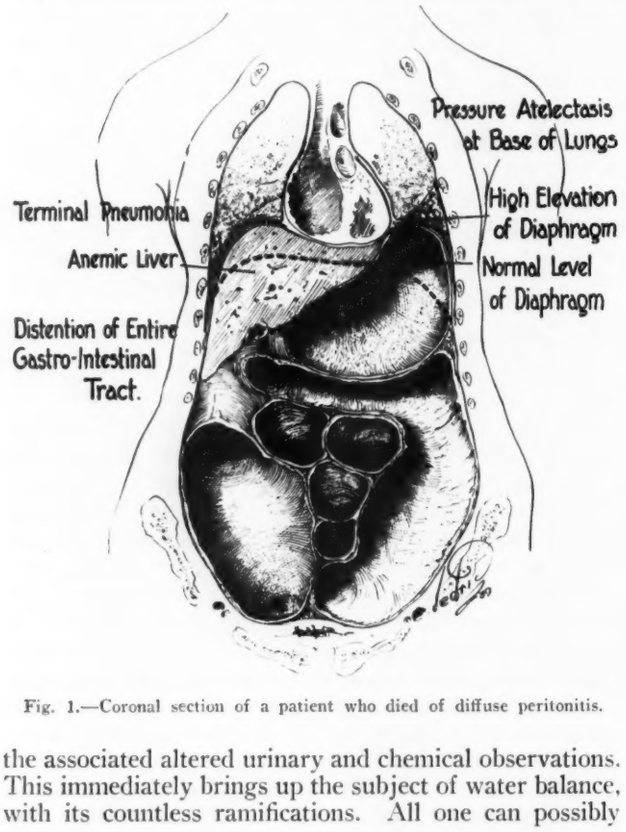

Fig. 1.—Coronal section of a patient who died of diffuse peritonitis.

the associated altered urinary and chemical observations. This immediately brings up the subject of water balance, with its countless ramifications. All one can possibly

TABLE 2.—*Blood Picture in a Case of Diffuse Peritonitis in Which Temporary Leukopenia, an Indication for Transfusion, Developed*

Date	Red Cells	Hemoglobin, Percentage	White Cells	Juveniles	Bands	Filaments	Lymphocytes	Monocytes
4-4-38	4,500,000	85	12,950	2	10	74	12	2
5			16,200	3	11	70	14	2
6	Trans. 750 cc.		8,250	6	18	65	14	3
7	4,300,000	85	11,650	6	18	65	9	2
8	4,350,000	80	13,500		15	71	14	
9	4,450,000	80	14,550		10	74	14	2

hope to do with fluids is to meet the increased metabolic needs and endeavor to keep the patient as nearly as possible in physiologic balance.

Prior to the renewed interest in the maintenance of water balance occasioned by Coller and Maddock,[2] we lost some patients because of dehydration. We have during the past few years been able to maintain patients even to the day of their death with a normal urine and a normal output and with normal blood values for urea, carbon dioxide combining power and chlorides. These are the only yardsticks at present with which one can measure dehydration, if indeed that is at all possible. Consequently, we administer just sufficient fluids to maintain the blood chemistry and urine within normal limits. As to the type of fluid, the blood chlorides are used as an index. Only a sufficient amount of saline solution is administered to maintain the blood chlorides at a normal level, with the remainder of the fluids given in the form of sterile distilled water. Early in our experience we produced edema by using more saline solution than was indicated physiologically. For the parenteral administration of fluids in the type of cases under consideration we employ the intravenous drip method exclusively.

The third adjunct is morphine. By the use of this drug one hopes to relieve pain, by far the most impor-

TABLE 3.—*Blood Picture in a Case of Diffuse Peritonitis with Persistent Leukopenia, an Indication for Multiple Transfusions*

Date	Red Cells	Hemoglobin, Percentage	White Cells	Juveniles	Bands	Filaments	Lymphocytes	Monocytes
1-6	4,730,000	90	4,200	1	45	40	13	1
7			5,400	2	42	35	18	3
8			3,300		40	42	16	2
9	4,600,000	85	2,500		56	38	13	3
10	5,000,000	85	6,100		28	50	12	
11	4,750,000	85	10,250		20	64	16	5
			Daily Transfusion of 800 Cc.					

tant object, keep the patient quiet, diminish peristalsis and at the same time increase the tone of the intestinal musculature and combat distention. If the drug is administered properly after several large initial doses at comparatively short intervals, the patient may get along without any morphine for from six to eight hours. A sudden cumulative action of the drug must be feared

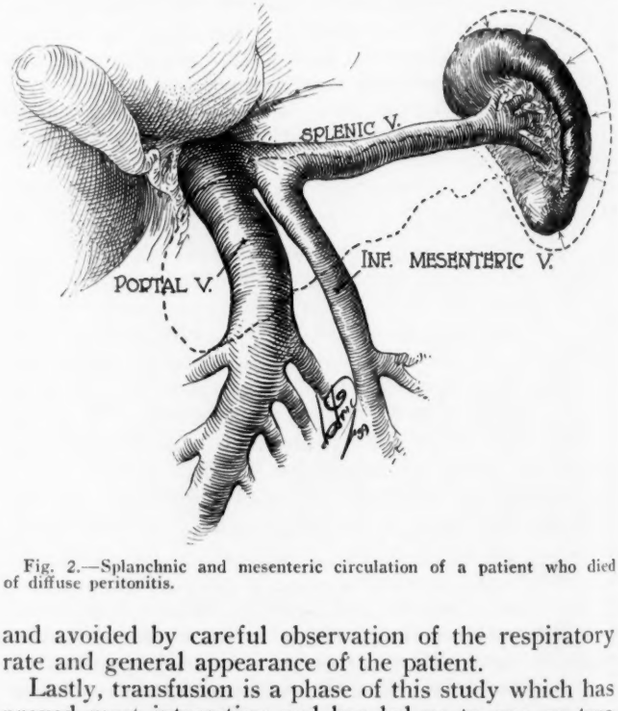

Fig. 2.—Splanchnic and mesenteric circulation of a patient who died of diffuse peritonitis.

and avoided by careful observation of the respiratory rate and general appearance of the patient.

Lastly, transfusion is a phase of this study which has proved most interesting and has led us to one or two observations which, as near as we are able to determine, have not been described before.

What are the indications for transfusion? The first is a slowly falling blood pressure associated with a gradually mounting pulse rate, regardless of the appearance of the patient. We have come to consider these

2. Coller, F. A.: Studies in Water Balance, Dehydration and the Administration of Parenteral Fluids, Minnesota Med. **19:** 490-494 (July) 1936. Coller, F. A.; Dick, V. S., and Maddock, Walter S.: Maintenance of Normal Water Exchange with Intravenous Fluids, J. A. M. A. **107:** 1522-1527 (Nov. 7) 1936. Coller, F. A.; Bartlett, R. M.; Bingham, D. L. C.; Maddock, W. S., and Pedersen, Svend: The Replacement of Sodium Chloride in Surgical Patients, Ann. Surg. **108:** 769 (Oct.) 1938.

signs as a warning that the patient is entering a condition of shock with more and more blood stagnating in the splanchnic and mesenteric systems and less being fed to the heart for the peripheral circulation. Transfusion should be performed at this stage, if it is to do any good, before the blood pressure becomes imperceptible and the pulse uncountable and a true circulatory

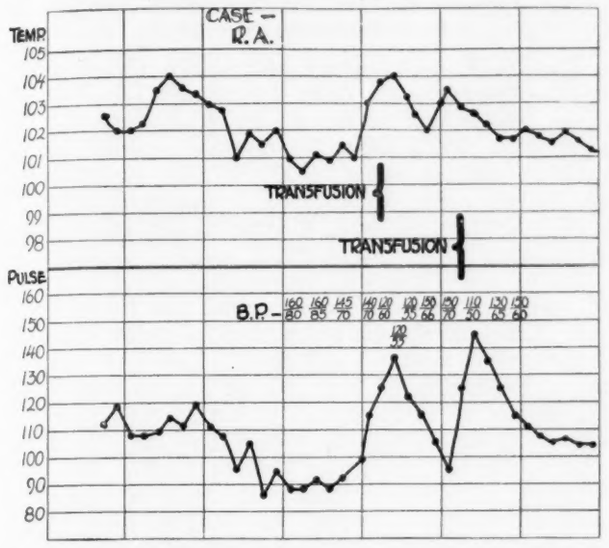

Fig. 3.—Changes in the pulse rate and blood pressure which indicate transfusion.

collapse occurs. By transfusion we increase the volume of circulating blood, attempt to restore the blood pressure and supply blood to the peripheral tissues.

The second indication for transfusion is a marked fall in the total white blood cell count. The explanation for this phenomenon is that that particular hemopoietic system is being overcome by the infection and its products and is failing to respond. Transfusion should be done at this time without delay and without waiting for any further developments. Otherwise the white blood cell count will continue to fall and the condition become beyond redemption. The bone marrow itself is evidently not primarily damaged, as is evidenced by its response to transfusion, but its function is temporarily suppressed and transfusion is a factor in stimulating it to renewed activity.

There is a perplexing type of blood response in certain cases of diffuse peritonitis, namely persistent leukopenia, with the count ranging from 1,500 to 4,000 and the appearance of an increased number of young forms, or a degenerative shift to the left such as occurs in other acute unfavorable infections. Regardless of how much blood is given, the blood picture does not return to normal until the patient has overcome the infection. We have given as much as 5,200 cc. of blood in five days with no change in the white cell or differential count until the patient was on the road to recovery. We feel that this is a point in favor of the theory that the activity of the bone marrow is merely suppressed by the overwhelming infection and not primarily damaged.

We use from 750 to 1,000 cc. of blood for the average transfusion given indirectly. No ill effects from the administration of such large quantities of blood given at frequent intervals have been noticed. The hemoglobin content, red blood cell count, icteric index, van den Bergh reaction and urine remain normal.

To apply the aforementioned principles, a more or less definite regimen of treatment had to be worked out for all patients with diffuse peritonitis. No one appreciates better than we the fact that medicine is much more than an exact science and that no definite rules for an entire group can be formulated because almost every case presents a problem peculiar to itself. It seemed, however, that a systematic plan embodying the foregoing principles might be formulated which would be applicable in most cases and still sufficiently flexible for individual variations. Consequently, during the past five years we have endeavored to fit every case as far as possible into the following plan:

No patient is sent to surgery until the shock, distention and dehydration are more or less successfully combated. We feel that by superimposing the shock of an operation, no matter how rapidly and gently it is performed, on patients already exhibiting to some degree the manifestations of shock, the mortality rate will be definitely increased. To correct these conditions will rarely defer operation more than two or three hours.

Every patient is returned from surgery with the following orders: A hypodermic of morphine sulfate 0.015 Gm. is administered for pain, restlessness and nausea. This is repeated as often as necessary, and the only contraindication is a respiratory rate of 12 or lower.

A continuous intravenous drip is instituted immediately, 10 per cent dextrose being alternated with 5 per cent dextrose in amounts to meet the individual requirements.

Duodenal decompression is inaugurated immediately.

The patient's blood is typed and cross agglutinated so that he may receive a transfusion without delay when the aforedescribed indications arise.

A complete blood count and urinalysis are performed daily.

The blood pressure and pulse rate are taken every hour.

There are daily estimations of the urea content, carbon dioxide combining power and chloride content of the blood.

Fifty cc. of 50 per cent dextrose is administered twice daily in an attempt to get an additional 50 Gm. of dextrose into the body every twenty-four hours as nutrition for the cardiac musculature.

The patient is placed in Fowler's position,[3] and nothing is administered by mouth.

These orders adequately take care of the routine procedures, and as the need for individual treatments arise, such as the use of oxygen, they can be ordered.

Fig. 4.—Average length of life of patients who died after operation in the two series of cases.

All that remained now was the practical application of the principles just discussed in a series of cases comparable in every respect with those reported in 1935 to prove whether or not these factors would influence our mortality rate. In this paper we are reporting sixty cases of diffuse peritonitis treated as we have outlined.

Cultures of the peritoneal exudate were taken in all but two instances, or in 96.7 per cent of the cases. Positive results were obtained in all. The various organisms reported were Bacillus coli, Streptococcus haemolyticus, Streptococcus faecalis, Bacillus aerogenes, Bacillus pro-

3. Fowler, G. R.: Sitting Position in the Treatment of Appendical Peritonitis, M. Rec. **57**: 617-623, 1900.

teus and Staphylococcus aureus. It is interesting to note the comparative absence of anaerobic organisms although definite attempts were made to demonstrate them in each instance. The pathologic reports confirmed the diagnosis of appendical involvement in all cases. The patients were ill at home before hospitalization an average of 72.4 hours. The physical examination in every instance confirmed the diagnosis of diffuse peritonitis. All were operated on by one of three surgeons, each familiar with the various standards and criteria set forth. The operative procedure was appendectomy and drainage in each instance. The average hospital stay of the patients who survived was 27.27 days.

We have outlined the requirements each case had to fulfil before inclusion in this series to show that in each and every instance we were dealing with a patient with diffuse peritonitis due to perforation of the appendix.

In this series of sixty cases we had seven deaths, representing a mortality rate of 11.7 per cent. One of these deaths, after an apparent recovery, was due to a volvulus necessitating a resection of 3 feet of small intestine. One patient bled to death from an erosion through a blood vessel in the cecum although his peritoneal cavity at the time of autopsy showed no evidence of peritonitis. The remaining five patients suffered no complications and died of peritonitis. All the patients were examined post mortem. Bacillus coli was reported five times, Streptococcus haemolyticus once and Staphylococcus aureus once. Blood cultures were negative.

TABLE 4.—*Diffuse Peritonitis, 1935-1939*

Cases	Deaths	Mortality, Percentage
60	7	11.7

Average time, onset to hospitalization, 72.4 hours

It is interesting to note that in the cases reported in 1935 the patients who died lived an average of only 4.2 days subsequent to operation. In this series the seven patients who died, treated as outlined, lived an average of 13.8 days subsequent to operative intervention.

A compilation of the mortality rate in the United States for diffuse peritonitis following perforation of the appendix made by Bower [4] revealed an average mortality rate of 33 per cent. Lied's clinic [5] in Norway published a mortality rate of 27.39 per cent. We believe that the procedures described, used for the indications we have mentioned, have reduced the mortality rate from diffuse peritonitis following perforation of the appendix in the Buffalo General Hospital and Buffalo Children's Hospital from 45.4 to 11.7 per cent.

40 North Street.

4. Bower, John O.: Spreading Peritonitis Complicating Acute Perforative Appendicitis, J. A. M. A. **112**: 11-17 (Jan. 7) 1939.
5. Haggard, W. D.: Surgery Queen of the Arts, Philadelphia, W. B. Saunders Company, 1935.

Density of World Population.—The average density of world population as a whole is nearly 41 persons per square mile, as we have seen. Yet the populations on over 81 per cent of the total land area are living at densities under 40. About 14 per cent of the population of the world—roughly one person in seven—is living at densities of 600 or above, that is with one acre or less per person, on an even personal distribution of area. —Pearl, Raymond: The Natural History of Population, New York, Oxford University Press, 1939.

APPENDICITIS: NEWER METHODS OF TREATMENT

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The 16,000 deaths every year in the United States from appendicitis are quite unnecessary. Early diagnosis and prompt treatment for appendicitis, as for diphtheria, should make the mortality from either of these diseases almost negligible. In late cases, however, the analogy limps, because late in diphtheria treatment is of practically no avail, whereas in the late stages of appendicitis proper treatment is usually successful.

In the early stages of appendicitis almost any kind of appendectomy will do, but in the late stages skilful technic and physiologic procedures frequently make the difference between life and death. Late and neglected cases result largely from lack of appreciation of the importance of early operation, but, though education may do much to lower the incidence of late cases, there will doubtless for various reasons always be a considerable number of them. A large percentage of patients with a ruptured or gangrenous appendix operated on at St. Elizabeth's Hospital have had a purgative for indigestion or abdominal pain. "Late" does not necessarily mean in point of time but connotes the progress of the pathologic lesion. An "early" appendicitis may with a purgative or an enema become "late" and gangrenous in twenty-four hours. The prevalence of the conservative or Ochsner treatment for acute appendicitis and the so-called freezing of the appendix by icebags to the abdomen are also responsible in many cases of appendicitis for the development of abscess or peritonitis.

TREATMENT

Since Jan. 1, 1931, we have adopted five points for the routine treatment of all patients with acute appendicitis:

1. Immediate operation is done as soon as the diagnosis is made, no matter what the stage of the disease.
2. A McBurney or gridiron incision is made, and the appendix is always removed. We have not left an appendix in during this period.
3. The tissues are handled gently, suction is used instead of sponges, and no gauze sheets or packs are placed within the peritoneal cavity.
4. The stump of the appendix is treated simply, being merely ligated, severed and disinfected.
5. Physiologic rest of the gastrointestinal tract is effected by limiting the oral intake and avoiding proctoclysis. In all cases of spreading peritonitis or when a perforation or abscess exists, essential water and electrolytes with some calories are given intravenously by 5 per cent dextrose in saline or Ringer's solution. If there is distention, the stomach is decompressed by inserting a nasal tube to the stomach or duodenum and, if the distention is great, continuous suction is applied.

While patients do not usually die within the first eight or nine hours from a gastrointestinal perforation, which a ruptured appendix is, they may acquire a fatal infection during this time unless there is prompt and

From the Surgical Department of St. Elizabeth's Hospital.
Read before the Section on Gastro-Enterology and Proctology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.

proper treatment. This is shown by the history of perforating peptic ulcers. It seems a good surgical rule to close a gastrointestinal perforation as soon as possible. No one denies the wisdom of removing an acutely inflamed appendix before it has ruptured.

If the appendix has ruptured and there is a local abscess, the abscess is opened as gently as possible without disturbing the adhesions except just enough to gain access to the appendix. A suction apparatus withdraws the pus. In peritonitis this is also done, but under no condition is gauze packing placed or sponging with gauze used to remove pus. A gauze sponge that removes some of the pus also forces into the tissues sepsis which otherwise might not be absorbed. It may not appear elegant to see pus running over the wound and the intestine, but it is much better than to press even a small portion of it into the tissues. If a suction apparatus is not available, a catheter with a syringe attached can be used.

The treatment of the stump of the appendix is simple. The base is ligated with stout chromic catgut but is never clamped. Clamping the base and placing the ligature in the bite of the clamp crushes the base unnecessarily, whereas the only tissue to be injured should be that within the grasp of the ligature, which makes a much narrower trauma than a clamp. The appendix is clamped a short distance from the ligature, surrounded with moist gauze and severed with the electric cautery. The stump is disinfected with pure phenol, curetted and again disinfected with pure phenol. The ligature on the stump is threaded in a needle and passed through adjacent peritoneum-covered fat. This is done to promote the absorption of the stump and to protect it from the pressure of the drainage. No sutures are placed in the cecum and no effort is made to bury the stump of the appendix.

The mortality rate in this series would seem to demonstrate that the arbitrary adherence to any so-called law of surgery is not always wise. To be sure, in suturing large wounds in the intestine the peritoneal surfaces should be brought together, but in a small puncture the mucous membrane frequently heals satisfactorily if approximated. This is not to say that the principle of uniting peritoneum to peritoneum is wrong, but in science there is no creed and no inviolable law, and the fact that a large wound of the stomach or intestine should be sutured so as to approximate the peritoneal coats does not necessarily imply that a small wound under different conditions should be treated in the same way. Willis [1] has shown that the mortality rate of intestinal wounds made by small shot is lower when no surgical operation is done and the perforations are not sutured than when there is a formal operation and the intestinal wounds are sutured. This is because in these small wounds the mucous membrane protrudes and stops the gap, and healing is satisfactory.

Burying the stump of the appendix creates a cavity in which necrotic material, the stump of the appendix and a foreign body, the ligature, are enclosed, and the purse-string suture which buries the stump cuts off some of the blood supply. This would seem to be an ideal method for creating an abscess, and as a matter of fact it apparently does. Thus, H. E. Robertson,[2] pathologist at the Mayo Clinic, has found that in all necropsies in cases in which the appendix has been removed incidentally during some other operation there is a pocket of pus in this cavity up to twenty-one days after the operation. Fortunately it usually ruptures into the intestine, but it may not always do so. Dr. Robertson says: "For a long time I have been, in season and out of season, inveighing against the custom of burying the stump of the amputated appendix. It strikes me as wholly illogical and, worse than that, a dangerous procedure. The well known ostrich with his head in the sand hasn't very much on this custom."

The McBurney incision gives ample access in most cases of appendicitis and can be enlarged if necessary. It is particularly adaptable in suppurative cases because in such instances the wound is not closed. One or two cigaret drains and a soft rubber tube are inserted, and the peritoneum is lightly sutured around the drains. The rest of the wound is left open and packed with petrolatum gauze. When such wounds are sutured, suppuration of the abdominal wound often follows and there are pockets of pus. This treatment has been advocated by H. A. Gamble of Mississippi in all cases of peritonitis. It is a valuable contribution.

The cigaret drains are left in for about two days, though if the temperature continues high and the pulse is rapid the drains are not disturbed until the temperature and pulse rate come down. Drainage is not solely mechanical, but the presence of the gauze cigaret tends to induce pouring out of lymph around it and washes out the sepsis. The petrolatum gauze is not removed for several days. The wounds usually heal satisfactorily and may be drawn together with adhesive tape.

So far as we know there have been in this series only six cases of postoperative hernia in 119 drainage cases, and they have all occurred in cases in which there was rather extensive, long draining sepsis.

The principles laid down by Hilton [3] in his classic work on rest and pain about 1863 still hold. Physiologic rest is one of the best therapeutic agents, and in order to apply it the function of an organ or tissue must be determined and either abolished or diminished as much as possible. Fluids are absorbed chiefly from the right half of the colon, and when proctoclysis is given it not only throws more strain on the site of the appendectomy but, instead of giving rest, incites peristalsis and burdens the adjacent intestine with increased absorption of fluids. When there is perforation, an abscess or peritonitis, the patient is given intravenously 5 per cent dextrose in Ringer's solution continuously, usually from 150 to 250 cc. an hour. If the blood pressure is low, this amount is increased. If the patient is quite ill we use an intravenous cannula instead of a needle, and the phleboclysis may be continued for several days. Nothing is given by mouth except a small amount of water. If there is distention a Jutte or a Levine tube is passed through the nose; then the patient may have water more freely if the tube is kept open.[4]

Five per cent dextrose in salt solution, in Ringer's solution or in distilled water may be now obtained in large ampules and if properly given almost never causes a reaction. Our statistics at St. Elizabeth's Hospital show that the incidence of pulmonary embolus after the intravenous use of this fluid is less than the average in many other hospitals, being 3.57 per cent of all deaths in surgical cases. It should be given without the so-called drip apparatus, merely a graduated glass

1. Willis, B. C.: Shotgun Wounds of Abdomen, with Report of Experimental Work, Am. J. Surg. **28**: 407-427 (May) 1935.
2. Robertson, H. E.: Personal communication to the authors.
3. Hilton, John: Lectures on Rest and Pain, London, George Bell & Sons, Ltd., 1920.
4. Horsley, J. S.: Continuous Intravenous Injections (Phleboclysis), Surgery **2**: 622 (Oct.) 1937.

container and a thumb-screw being used to regulate the flow. The drip device is not only unnecessary but is positively dangerous. Terplan,[5] before the Buffalo Pathological Society, reported a case in which sudden death followed the intravenous drip of 5 per cent dextrose solution and necropsy showed air trapped in the main stem of the pulmonary artery. When the patient strains and the venous pressure is high the fluid is forced back; when the patient suddenly ceases to strain some of the air that has been compressed in the drip apparatus may be sucked in. It adds an utterly unnecessary complication to the administration of a very effective therapeutic agent, because the rate of flow can be regulated more accurately by the graduated container than by the drip.

The patient is propped up in bed and an adequate amount of morphine is administered at regular intervals. In many of the drainage cases hot dressings of supersaturated solution of boric acid are applied over the abdomen. Neither enemas nor purgatives in any form are used until the patient is out of danger.

In our series there have been four cases of fecal fistula; all of them have healed satisfactorily within three weeks from the time of their appearance, with no further operative treatment.

Unless all these five points are followed, it would doubtless be unwise to adopt some of them, such as the removal of the appendix in every case and immediate operation. Some of these five points, such as the McBurney incision, immediate operation and the simple treatment of the stump of the appendix, have been used by us for many years before 1931, but it is only since that time that they have been combined with two other extremely important points; that is, giving physiologic rest by supplying fluids intravenously, and the use of suction for removing pus instead of sponging or placing gauze packs in the abdomen.[6]

We seldom encounter paralytic ileus or mechanical obstruction. When distention does occur we use the nasal tube with suction, phleboclysis and an oxygen tent with high concentration of oxygen. The benefit of the

TABLE 1.—*Appendectomies at St. Elizabeth's Hospital Jan. 1, 1931, to May 1, 1939*

	Cases	Deaths	Per Cent
Acute appendicitis	621	4	0.64
Acute appendicitis with peritonitis	119	2	1.68
Subacute and recurrent chronic appendicitis	231	0	0
Carcinoid	1	0	0
	972	6	0.617

use of sulfanilamide in appendicular abscess or in spreading peritonitis from appendicitis has not been definitely determined. Primary or hematogenous peritonitis is frequently from streptococci, and here sulfanilamide is extremely helpful. A patient treated by one of us (J. S. H. Jr.) who had a primary peritonitis and who was given sulfanilamide freely recovered with remarkable promptness. This was dramatic, but though the preoperative diagnosis was appendicitis the appendix was not diseased and the offending organism was the hemolytic streptococcus. In appendicular peritonitis the colon bacillus (Escherichia coli) usually dominates and sulfanilamide has little or no effect on it. If streptococci occur abundantly in the infection it might be well to use sulfanilamide. While we have given sulfanilamide to some of these patients, the difference between their convalescence and the convalescence of those who were not given sulfanilamide is not impressive. It must be borne in mind that large doses of sulfanilamide may not be innocuous.

When no drainage is used the patient is kept in bed about nine or ten days and a few days later is permitted to return home. The practice of getting a patient up the second day after operation and having him leave the hospital on the third day is more spectacular than scientific. It has been well demonstrated that wounds in the intestine are weaker the second or third day than in the first twenty-four hours and then they gradually become firm again. While of course the procedure of having the patient up two or three days after the operation is spectacular and in many instances can be done without injury, it seems highly probable that if the convalescent is kept at rest for a sufficient time for firm healing of the wound the subsequent complications and sequelae will be fewer. Ogilvie[7] of London, a distinguished authority on surgery and a learned physiologist, said in a Mayo Foundation lecture in 1937:

> As a physiologic mechanism the abdominal wall demands activity. As an injured structure it requires rest for repair and relief from strain for security. A well sutured wound has a tensile strength of about 40 per cent of that of the tissues before they were cut. During the first few days the tissues undergo autolysis, while the sutures are being digested. By the fourth day the strength of the wound has sunk to some 20 to 25 per cent of the original. From the fifth day onward fibroblasts are laid down rapidly and the strength increases, so that by the sixth day it is 50 per cent and by the tenth day about 90 per cent of the normal. . . . But to allow or force him [the patient] to walk before the tenth day is to permit physiologic idealism to override pathologic common sense.

TABLE 2.—*Appendectomies at St. Elizabeth's Hospital Jan. 1, 1931, to May 1, 1939, for Acute Appendicitis*

	Cases	Deaths	Per Cent
Acute without perforation	621	4	0.64
Acute perforated:			
(*a*) Abscess and localized peritonitis	85	1	1.18
(*b*) Spreading peritonitis	34	1*	2.94
	740	6	0.81

* This patient also had a gangrenous intestine at the time of operation.

Our report covers a period of eight years and four months, from Jan. 1, 1931, to May 1, 1939, and includes all the cases in which disease of the appendix was the sole or the chief reason for the operation. Cases in which the appendix was removed incidentally to another operation are not included in this list. There have been 972 cases with six deaths. Of these, only one patient, whose intestine was also gangrenous, died of peritonitis. A brief summary of these deaths follows:

REPORT OF CASES

CASE 1.—A white woman aged 34 had retroversion of the uterus and what appeared to be acute appendicitis. The appendix was removed, but an abscess was found in the left ovary and tube which involved the ileum so closely that it was necessary to resect some of the ileum. The abscess was in no way connected with the appendix, though the appendix showed acute inflammation. Intestinal obstruction and a localized left-sided peritonitis developed and the patient died five days later. The

5. Terplan, Kornels: Air Embolism with Unusual Sources and Pathologic Features, Arch. Path. **22**: 716 (Nov.) 1936.

6. Horsley, J. S.; Horsley, J. S., Jr., and Horsley, G. W.: Appendicitis: Its Diagnosis and Improved Methods of Treatment, Virginia M. Monthly **65**: 207-213 (April) 1938.

7. Ogilvie, W. H.: The Place of Physiology in Clinical Teaching, Proc. Staff Meet., Mayo Clin. **13**: 394 (June 22) 1938.

prime cause of death was not appendicitis, but since the appendix showed acute inflammation it is included in this series.

CASE 2.—A white man aged 84 complained of pain in the right side of the abdomen which was not well localized but was more prominent over the upper and lower portions of the right side of the abdomen than elsewhere. Under local anesthesia his appendix was removed and the tip was found to be high up almost under the liver. It was very adherent. At the tip was a concretion, and the appendix around this showed some inflammation though no actual pus. It was thought that this high location of the appendix accounted for the pain in the region of the gallbladder. Fourteen days after the operation the patient died. Necropsy showed a partly gangrenous gallbladder filled with pus and containing a very large stone. This condition was obviously present at the time of the operation but the diagnosis was missed because of the location of the appendix and because under the circumstances it did not seem advisable to make an incision over the gallbladder, which had originally been contemplated.

This patient, too, died from something not connected with the appendix. It was a case of missed diagnosis. It might be permissible to omit this case from the statistics of deaths from appendicitis, but on the whole it is probably better to include both of these cases.

CASE 3.—A white man aged 59 had a gangrenous appendix removed with satisfactory recovery except for slight pleurisy on the tenth day. He was preparing to go home when he died suddenly from pulmonary embolism on the sixteenth day after operation.

CASE 4.—A white man aged 50 had acute appendicitis. He had taken laxatives and purgatives. He was obese and chronically addicted to alcohol. The appendix was not ruptured but was acutely diseased. He died of uremia on the sixth postoperative day. The necropsy showed no peritonitis. There was cirrhosis of the liver and acute nephritis.

CASE 5.—A white man aged 72 had acute appendicitis with a retrocecal appendicular abscess. There was little pain and it was thought that the lesion was a cancer. Operation showed an abscess. The appendix was removed and the abscess drained. There was an exacerbation of chronic bronchitis with pulmonary edema. This was apparently controlled, but it recurred in forty-eight hours and the patient died five days after the operation with paralytic ileus and pulmonary edema. There was no spreading peritonitis.

CASE 6.—A white girl aged 17 years was brought to the hospital in rather a desperate condition. She had been delivered of a normal pregnancy three weeks previously. She complained of pain in the right side which had been present four days. There was a large amount of pus in the urine and at first it was thought that she had pyelitis. At operation there was a ruptured appendix, spreading peritonitis and about 3 feet of gangrenous intestine. The appendix was removed and the gangrenous intestine was resected. The patient died eight days later with an overwhelming infection.

With the six deaths in 972 cases there is a mortality rate of 0.617 per cent. If the first two cases mentioned are excluded from the deaths from appendicitis, the mortality rate would be 0.41 per cent.

The following six cases are briefly reported as illustrations. All of the patients recovered satisfactorily.

CASE 7.—A baby girl aged 8 months had severe abdominal pain, with a temperature of 102.5 F., a pulse rate of 176 and a white blood cell count of 27,800, with 70 per cent neutrophils. A large gangrenous appendix in a mass containing an abscess was removed. The patient is in good condition now.

CASE 8.—A white girl aged 4 years had acute appendicitis of about thirty-six hours' duration. On admission to the hospital the temperature was 104 F., the pulse rate 130 and the white blood cell count 20,000 with neutrophils 89 per cent. At operation there was extensive spreading peritonitis, and the appendix, which pointed toward the umbilicus, had ruptured near its tip. There were very few confining adhesions and the contents of the appendix emptied freely into the peritoneal cavity. The appendix was removed and the usual treatment was given. No sulfanilamide was administered. The patient was rather ill for several days. Her highest temperature the day after operation was 104 F. and the pulse rate 138. Three days after operation the temperature was 100 F. and the pulse 110. From that time on she made a satisfactory recovery. There was no hernia and the patient is now in excellent condition.

CASE 9.—A white boy aged 4 years had a rigid and distended abdomen and a large mass in the lower portion of the abdomen. The white blood cell count was 35,000, temperature 103.8 F., pulse 144. There was a ruptured appendix, a large abscess containing about 250 cc. of pus and extensive spreading peritonitis. The appendix was removed and the peritoneal cavity drained. The temperature the following day was 103.2 F. and the pulse from 140 to 150, but these became about normal after five days. There was a flare-up of temperature on the tenth day, but it returned to normal on the fourteenth postoperative day. The patient had some fecal drainage for about eleven days following operation, but the fistula healed and he was discharged from the hospital on the twenty-third postoperative day. He has remained well.

CASE 10.—A white man aged 33 had a temperature of 99.2 F., a pulse rate of 88 and a white blood cell count of 12,800, with neutrophils 87 per cent. There was a mass in the lower right quadrant of the abdomen. Nine months before admission to St. Elizabeth's Hospital an appendicular abscess had been opened and drained elsewhere but the appendix was not removed. The appendix was removed from very dense adhesions. The wound was drained. There was a fecal fistula for a while, which closed spontaneously. The patient left the hospital thirty-three days after the operation and when heard from recently he was in excellent condition.

CASE 11.—A white man aged 27 had a large mass in the lower right side of the abdomen; the temperature was 99.4 F., pulse 96 and white blood cell count 20,000. A gangrenous and ruptured appendix was removed from an abscess. Convalescence was uneventful except for drainage of some fecal material which began on the eighth postoperative day and closed before the patient was discharged from the hospital on the twenty-eighth day after admission.

CASE 12.—A white man aged 20 on admission had a temperature of 102.2 F., pulse 120, respiratory rate 24 and white blood cell count 14,800, with neutrophils 89 per cent. Two months previously he had been treated conservatively by his physician and dismissed. Then he entered another hospital and a diagnosis of acute appendicitis with abscess was made and the patient was treated by the Ochsner method. Later the abscess was drained through the rectum. He was dismissed from the hospital and went home but continued to have a fever. Twelve hours before admission to St. Elizabeth's Hospital he had a severe attack of acute appendicitis. At operation there were very dense adhesions, a large amount of foul pus and spreading peritonitis with rupture of a pelvic abscess which contained the appendix. The appendix, gangrenous and ruptured, was removed. The patient nine months after the operation is in excellent condition and free from symptoms, and there is no postoperative hernia.

SUMMARY

In the period from Jan. 1, 1931, to May 1, 1939, 972 patients have been operated on by the surgical staff of St. Elizabeth's Hospital for appendicitis. Every patient with acute appendicitis or peritonitis from appendicitis was operated on as soon as the diagnosis was made, and in every case the appendix was removed at the time of operation. The advantages of this over the expectant or conservative treatment or over treatment in which the abscess is opened and the patient returns home to have the appendix removed later are obvious. Not only the mortality and the morbidity rate but the financial burdens on the patient are lessened. However, immediate operation and removal of the appendix must depend on the other points, on the use of suction, giving the intestine a rest by intravenous injection instead of

proctoclysis, handling the tissues gently and simple treatment of the stump of the appendix. The examples that have been given show some of the desperate cases that we have had. Not one of the deaths was due to peritonitis except in one case in which it was necessary at the time of operation to resect gangrenous intestine.

It would seem that the general biologic principles that have been followed here should greatly reduce the morbidity and the mortality in the late cases of acute appendicitis.

617 West Grace Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. J. S., J. S. JR. AND G. W. HORSLEY AND DRS. WRIGHT, AARON, REGAN AND MILCH

DR. FREDERICK A. COLLER, Ann Arbor, Mich.: The mortality rate of acute appendicitis is much higher than it should be and there has been little if any improvement in the results of treatment of the disease in the last twenty-five years. The proper treatment for the disease is removal of the appendix while the infection is still limited to the appendix. Patients die from complications and not from acute appendicitis. If the diagnosis were made early and the appendix removed, the mortality would be negligible. I believe that obstruction of the appendix plays an important role in initiating the sequence of events as they occur in acute appendicitis. Studies in our clinic showed definite evidence of obstruction in 93 per cent of appendixes the site of acute infection. The diagnosis of appendical obstruction, the initial stage of acute appendicitis, can be made without leukocytosis and fever, and treatment carried out then will prevent complication. Another cause of delay in making the diagnosis of acute appendicitis is a not uncommon belief in the existence of vague entities such as "abdominal flu," food poisoning and food idiosyncrasies. Let us not wait for peritonitis with its fever and high leukocytosis before we make the diagnosis. The use of cathartics and purges for abdominal pain probably is the greatest single cause for peritonitis. There is the greatest difference of opinion as to the correct way to handle peritonitis. Shall we remove the appendix immediately or shall we defer operation while the patient is brought back to normal chemical balance? My experience is in accord with that of Drs. Wright, Aaron, Regan and Milch. I found that the mortality was entirely in the patient with diffuse peritonitis secondary to appendicitis. We removed the appendix in these patients in a routine way shortly after admission to the hospital with a mortality in that group of over 40 per cent. Ten years ago we began to follow the policy of deferring operation until the dehydration, hypochloration and ketosis were corrected, with a resulting diminution in the mortality of that group to about 8 per cent. I am unable to see anything new in the Horsleys' approach to the treatment, as what they advise is still the common form of treatment in this country. They are so skilful that their results are better than those usually obtained by others following the same method. I disagree with their advice always to remove the appendix immediately on seeing the patient. A patient with widespread peritonitis who has been vomiting and sick for from three to five days is the worst possible subject for an anesthetic and an operation.

DR. SIDNEY A. PORTIS, Chicago: The high mortality associated with acute appendicitis should not necessarily be laid at the door of the surgeon but should be brought home to the general practitioner or internist who first sees these patients and procrastinates before operative intervention is done. Fever has been regarded as a critical feature of this disease, and frequently one resorts to the use of mouth temperatures, which may be relatively normal, when elevations may be more accurately determined by the routine taking of rectal temperatures. I wish to add a note of warning against the indiscriminate use of fluids in cases of peritonitis. These fluids should not be given too rapidly. Pouring fluid into the veins may produce a right ventricular heart failure, with resulting passive hyperemia of the liver. This may affect liver function, and since one tries to preserve liver function in the treatment of infections, one may be defeating one's purpose by overzealousness in giving too much fluid. Too much chloride should not be given to patients because it may produce a tissue edema. The amount of chloride intake should be very carefully evaluated for each case.

DR. NIELS C. KLENDSHOJ, Buffalo: It has been my privilege to observe the work on diffuse peritonitis following appendicitis with perforation which Dr. Wright and his associates have presented. Irrespective of the controversial issues from the surgical standpoint, the main value of this work lies in the study and understanding of the altered physiology in these cases and the use of available means to combat such changes. Dr. Wright and his associates did not bring up very many of the laboratory data which they have on these patients, and I should like to add a point or two. These patients, when brought to the hospital, usually present a markedly lowered carbon dioxide combining power. This is not a primary condition but rather secondary, a result of severe dehydration and failure of the kidneys to eliminate and help maintain normal acid-base balance of the body. One of the complicating factors is that these patients, when brought to the hospital, have been sick for quite some time and may have had repeated emesis. This condition tends to produce alkalosis, and it is quite possible that this may alter the reported carbon dioxide figure toward a more normal value and thus give the surgeon a false sense of security. The actual loss of total base in these cases may quite well exceed what one might superficially estimate on the basis of the carbon dioxide figure.

DR. SARA M. JORDAN, Boston: I should like to congratulate the Program Committee on this symposium on appendicitis, which obviously needs to be presented often at these meetings, and I am glad the gastro-enterologists have it today. The papers which were given here today show the statistics on peritonitis. The excellent presentation by the Horsleys and by Dr. Wright and his associates show us what we have to face if we neglect the diagnosis. I should like to rise in defense of the surgeon as Dr. Portis did, to say that there probably is no problem in medicine which requires greater discretion than in the matter of the decision when to operate for appendicitis and when to consider the condition on a neurogenic basis. The problem of avoiding unnecessary appendectomies is not always simple and where there is doubt as to the presence of organic disease in the appendix it is, of course, much the lesser of two evils to operate and treat postoperatively for a functional condition than to delay surgery until complications have occurred.

DR. M. PINSON NEAL, Columbia, Mo.: Are we discussing appendicitis or its complications? It makes a great difference whether one is content to ride along with the "horse and buggy" diagnosis and include the complications with the disease, or whether one separates true appendicitis from the complications that arise through neglect, delay or improper treatment, often self administered. Any one who makes a diagnosis of appendicitis and not of its complications and then sits on the sidelines and watches is making a costly mistake. The authors opened but did not emphasize a most important yet an old story, the unwarranted condemnation of the blood count. A common error is to depend on the total leukocyte count, which is often noninformative or misleading. Frequently patients are kept under observation because a total leukocyte count was recorded as around or below 10,000. In a series of more than 1,800 consecutive operative patients having acute, suppurative appendicitis, diagnosed histopathologically, that I have studied, it was found that in more than 11 per cent the total count was 10,000 or less. If such a total count is accepted as diagnostic or as a criterion for surgical operation, these patients are without a friend at court. For a leukocyte count to be of value, there must be an estimation of polymorphonuclear neutrophil percentage to determine the presence or absence of infection, combined with a determination of the total number of leukocytes to weigh the patient's resistance, if infection is present. Our members are not wholly responsible for many deaths from appendicitis. The individual member of the population at large has an obligation in combating his or her disease. We must accept the responsibility for educating the public that when one has a bellyache, one must not attempt to freeze or cook the pain out. It is not to be treated by poultices, plasters or adjustments, pain relieving drugs, food or drink. Purgatives, laxatives or cathartics are not to be taken. If that bellyache lasts for two

hours or longer, a competent physician is to be called and given full responsibility. Our profession and the public must be emphatically told that for acute appendicitis there is only one route, the surgical one, and that delay is dangerous.

DR. J. SHELTON HORSLEY, Richmond, Va.: Dr. Neal has made a very important contribution to the discussion of this subject. I have not infrequently seen, as he has said, a case of ruptured, gangrenous appendix, with a leukopenia. That is the exception, but the laboratory man should not bear the brunt of this. It is like taking the temperature of a patient. You can't make a diagnosis solely on temperature, but, associating it with other symptoms, it is very helpful. Diffuse peritonitis and spreading peritonitis are merely different names for the same thing. There was only one death in spreading or diffuse peritonitis, and that was of a patient with a gangrenous loop of bowel which had to be resected. Our records show the results. We have had many patients recover who were very ill of the type that formerly on the old treatment usually died. In regard to the intravenous administration of fluid Dr. Coller has done more than any one else to show the importance of treating dehydration. The so-called intravenous drip is extremely dangerous, as has been explained in our paper. Unless all of these five points are followed, one should not operate at once on every patient or always take out the appendix. But when suction is used constantly the adhesions may be broken up, not freely, but enough to remove the appendix in every case, and then the complications are less. In this series of nearly a thousand cases we have had not a single case of subdiaphragmatic abscess. When an appendical abscess is merely drained and the patient sent home, the patient may or may not come back and frequently does not come back until there is another abscess, and what will one do then, keep on opening it? The only real test of new procedures is the death rate and the morbidity. We frequently have cases that have been treated elsewhere; in some of them an appendical abscess has been drained, and some have been treated medically. In every case that we have, whether there is diffuse or spreading peritonitis or if the patient seems moribund, the patient is operated on immediately, day or night. So our report represents every case we have. No one is permitted to die medically.

DR. A. H. AARON, Buffalo: We are dealing with one phase of the subject, diffuse peritonitis resulting from ruptured appendicitis. That confusion exists with regard to the treatment of ruptured appendicitis is evidenced by the following: Recently a group of senior students heard a presentation on the treatment of peritonitis following a ruptured appendix in which the speaker was quite clear that he was discussing only diffuse peritonitis of several days' duration. Nevertheless the senior students when asked the question "If you were entirely responsible for the care of a person whom you saw at 8 o'clock in the morning and your diagnosis was a possible acute appendicitis but for some reason decided to delay surgery and you returned at 4 o'clock in the afternoon, at which time in your opinion the appendix had ruptured, what would you do?" to our consternation said they would not operate but would treat the peritonitis. If there was one person who required surgery, it was this individual. Sir William Osler said years ago "There is no medical treatment of acute appendicitis." This still holds good. There is a medical preparation during the period of deferment of surgery for people with peritonitis, but there is nothing here that should be carried away, leaving in our minds an idea of delaying for one minute surgical intervention in the treatment of appendicitis. The treatment of this condition must be individualized, but I am certain of this one point: We must not have any misconception of what we are discussing. We are talking about diffuse peritonitis, not spreading peritonitis. Why do I believe in this modification of the treatment? Because the people live, as you saw, many days more than they did in our early group of peritonitis patients, who died within two or three days after they came to the hospital. In other words, we prolonged the life of a person with peritonitis to the extent of almost twelve days, in contradistinction to our early group of about three or four days, thus giving the patient an opportunity to develop and utilize his own protective mechanism to bring about recovery.

TUBERCULOSIS OF THE KNEE IN INFANCY AND CHILDHOOD

FRANCIS M. McKEEVER, M.D.
LOS ANGELES

No controversy exists concerning the treatment of tuberculosis of the knee joint in the adult. The value of surgical procedures to produce femorotibial synostosis in the general management of a tuberculous knee in the period from young adult life to middle age is no longer debatable.

For the aged there is also reasonable agreement that amputation at the thigh is the logical procedure.

The highest incidence of tuberculosis of the knee joint is, however, in infancy and childhood. It is in the years of growth, while epiphysial cartilages are still present, that there is a lack of agreement as to the place of surgical measures in the treatment of this condition.

During the period from birth to epiphysial closure, any surgical measure which encroaches on the articular portions of the tibia and femur has been looked on with distrust by the majority of surgeons. Girdlestone,[1] after circularizing fifty-five orthopedic surgeons in Great Britain, continental Europe and North America, stated that the operation of resection for arthrodesis should not be performed before the age of 15. Calvé [2] has expressed the majority opinion in the terse sentence "One commits a grievous blunder in resecting the knee of an infant."

The protagonists of operations to produce an arthrodesis of the knee in infancy and childhood have been few in the last forty years. They are, for the most part, surgeons in the British Isles. Sir William Thompson,[3] writing in 1905 after thirty years' experience with the operation of resection, remained a stanch advocate of early surgical arthrodesis regardless of age. Sir Harold Stiles [4] in 1912, after a careful study of the end results in thirty cases followed for several years, advised resection aimed at producing bony ankylosis in this age group and condemned all surgical intervention which did not have this end. Sixty-two per cent of his patients were subjected to ankylosing operations before the age of 6 years and 100 per cent prior to the age of 12 years. Despite Stiles's good end results, resection of the knee in children was looked on with disfavor through the next quarter century.

Tregubov,[5] analyzing the trend of opinion in 1937, found most surgeons still prejudiced against this type of operation. At this time he mentioned only Maffei and Kornev as approving of resection of the knee prior to the age of 12 years. The author himself leans slightly toward the procedure and has tried resection in a few children.

Those who advocate withholding from the infant a procedure which has proved of definite value to the adult with the same disease do so on two grounds: 1. Tuberculosis of the knee in the child heals under conservative treatment. 2. The shortening and deformity

From the Orthopedic Department, Children's Hospital.

Read before the Section on Orthopedic Surgery at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. Girdlestone, G. R.: The Pathology and Treatment of Tuberculosis of the Knee Joint, Brit. J. Surg. **19:** 488-507 (Jan.) 1932.
2. Calvé, J., and Galland, M.: Resection du genou pour arthrite tuberculeuse, Marseille-méd. **17:** 1003-1020 (June 15) 1925.
3. Thompson, Sir William: Operative Methods—New and Old—in Tuberculosis of the Knee Joint, Brit. M. J. **1:** 68-72 (Jan. 14) 1905.
4. Stiles, Sir Harold: Discussion on the After-Results of Major Operations for Tuberculous Disease of the Joints, Brit. M. J. **2:** 1356-1364 (Nov. 16) 1912.
5. Tregubov, S.: Operative Treatment of Tuberculosis of the Knee Joint, J. Bone & Joint Surg. **19:** 734-745 (July) 1937.

resulting from resection in the child are too crippling to justify the procedure. There are, however, no convincing statistics that proved tuberculosis of the knee in the infant and the child heals spontaneously or differs in its clinical course from tuberculosis of the knee in later years.

The shocking character of the deformities resulting from the old time massive excisions is undoubtedly responsible for the second objection. Despite the many defenders of conservative treatment for the child, there are many evidences of dissatisfaction with this policy of appeasement. This is attested by the constant appearance of compromising surgical procedures which leave unblemished the articular cartilages of the knee joint, such as the Robertson-Lavalle [6] operation, directed at increasing circulation in the tuberculous area; the femur-patella-tibia arthrodesis of Delehaye; [7] the "clavettage" of Yvin; [8] synovectomy, and lumbar sympathectomy. The development of these procedures and their acceptance for trial by surgeons indicate that the results of purely conservative treatment of tuberculosis of the knee joint in the child have not been entirely satisfactory.

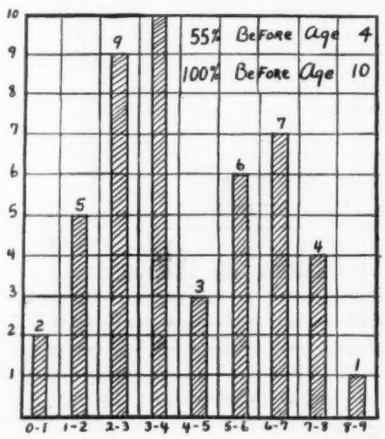

Fig. 1.—Age incidence.

PATIENTS STUDIED

Forty-seven patients were studied, all suffering from tuberculosis of the knee, proved to be that disease and no other by the recovery from the knee of either tubercle bacilli or tissue with the typical microscopic picture of tuberculosis. These patients were studied to determine the results of conservative treatment and of operative treatment directed toward producing a femorotibial synostosis. Under conservative treatment are included traction, the use of casts or braces and all operative measures which do not remove the articular cartilage from the adjacent surfaces of the femur and tibia, such as synovectomy, extra-articular excochleation of a tuberculous focus in the bone, lumbar sympathectomy and extra-articular fusions.

Under surgical treatment are included all operations designed to produce bony ankylosis between the femur and the tibia. The initial surgical procedure in all cases consisted of a removal of the easily available synovial membrane in the joint and suprapatellar pouch. The articular cartilage was removed from the ends of the femur and tibia until the cancellous bone of the ossification centers presented itself, the epiphysial lines being avoided. All tuberculous foci encountered were thoroughly curetted and emptied, even though they crossed the epiphysial lines. No attempt was made, however, to eradicate all disease. In none of the operations was internal fixation used to maintain position.

6. Robertson-Lavalle, Carlos: Le traitement des ostéo-arthrites tuberculeuses du genou, Rev. d'orthop. **11**: 5-19 (Jan.) 1924.
7. Delehaye, A.: Treatment of Quiescent Tumor Albus and Pseudarthrosis of Tuberculous Origin in Children, J. Bone & Joint Surg. **18**: 51-54 (Jan.) 1936.
8. Yvin, P.: Use of Tibial Graft in Arthrodesis in Children, Presse méd. **44**: 516-517 (March 25) 1936.

The age incidence of the disease in these patients is of interest with regard to treatment. Twenty-six patients, or 55 per cent, presented clinical manifestations of their illness before the fourth year of life had been completed. The remaining twenty-one, or 45 per cent, manifested their infirmity before reaching their tenth year of life. The appeasement policy of withholding resection until the completion of growth of the long bones would have required six years of treatment for the entire group and eleven years of treatment for more than 50 per cent. These children under conservative treatment, even if it had resulted in an arrest of the tuberculous process, would have grown up under the marquee of a hospital or clinic with the threat of an exacerbation hanging over them and the expectancy of a definitive surgical operation at the end of this road.

The academic question of the initial site of disease in tuberculosis of the knee has been pretty well reduced to the fact that by the time there is clinical evidence of the illness both the bone and the synovial membrane are involved. In this group of forty-seven children fifteen, or 31.9 per cent, almost a third, exhibited roentgenologically a definite bone abscess, sometimes very extensive, in either the lower end of the femur or the upper end of the tibia. This tuberculous abscess often involved both the metaphysis and the epiphysis and transgressed extensively on the epiphysial line early in the disease.

RESULTS OF CONSERVATIVE TREATMENT

A total of 137 years of conservative treatment employed for forty-six patients, or an average of three years per patient, did not result in one knee joint which did not show clinical signs of active disease or which permitted the patient to be about without apparatus of some type. The shortest period of conservative treatment was one month and the longest nine years. After various periods of appeasement it was possible either to recover tubercle bacilli from or to demonstrate the tubercle microscopically in thirty-nine of these patients who were subjected later to resection.

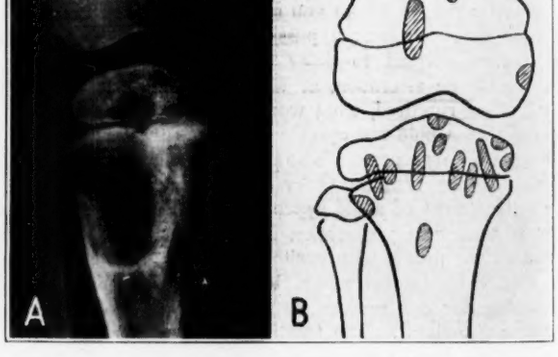

Fig. 2.—*A*, large tuberculous abscess involving metaphysis and epiphyses; *B*, sites of fifteen bone foci in forty-seven patients.

Two patients died under strictly conservative treatment, one from pulmonary miliary tuberculosis after two years of the disease and the other from tuberculous meningitis after one year of the disease.

One patient, under nonsurgical treatment, came to amputation after two years of illness; in another case,

because of the extensive dissemination of tuberculosis through the soft tissues, amputation was advised but refused.

Draining sinuses developed spontaneously in five patients under conservative treatment.

Other surgical tuberculous foci developed in two patients under conservative treatment.

Fig. 3.—Resection had been performed six years before, at the age of 9 years.

Synovectomy alone was resorted to twice without influence on the course of the pathologic process.

Lumbar sympathectomy was employed twice. In both patients the clinical signs of activity seemed to increase rapidly. Whether this resulted from the compromising surgical intervention or occurred in spite of it is conjectural.

Extra-articular arthrodesis by means of lateral grafts was carried out in one case with the production of a structural disturbance in the femoral and tibial epiphyses and a severe flexion deformity of the knee. The disease, however, was not arrested.

One child was cured by conservative surgical treatment, and eight years after the extra-articular excochleation of a tuberculous abscess in the tibial epiphysis had a knee joint with normal motion and no clinical or roentgenographic evidence of tuberculosis. Excochleation was used in all in six cases, but in five, despite the improvement in the bone focus, the tuberculous process extended into the knee joint.

RESECTION

Thirty-nine patients were subjected to an "economical resection" aimed at producing a femorotibial synostosis. The majority of the resections were carried out between the sixth and eighth years, thirteen patients being operated on in this interval. On the oldest the operation was performed in the tenth year of life and on the youngest at the age of 17 months. The latter operation failed completely, resulting in motion. Activity of the disease continued and the knee was finally arthrodesed by a second operation in the tenth year. Two of these patients died as a direct result of the operation.

One, a 7 year old boy, died suddenly at operation, shortly after the removal of the tourniquet. The operation was not prolonged and his condition was good throughout. Autopsy revealed a pulmonary embolus. The other, a boy of 3½ years, died ten days postoperatively, with an extensive cellulitis involving the entire thigh, and a blood culture showed Streptococcus haemolyticus. He was subjected to resection two weeks after a biopsy. The biopsy incision was not soundly healed and gaped slightly with granulation tissue. This death might have been avoided had sufficient time been permitted to elapse for the biopsy wound to heal.

The mortality of the entire group of patients was 8.5 per cent. The mortality from resection alone was 5.1 per cent.

RESULTS

Of the thirty-seven patients who survived resection it was possible to trace thirty-four for from one and a half to thirteen years. At the time of the study of end results 42.4 per cent were over 14 years of age, so that little chance for further disturbance of growth remained.

Of the thirty-four patients whom it was possible to follow, thirty-one, or 90 per cent, were in excellent general health. One patient, at the age of 17, despite the fact that his knee had been solid for thirteen years, had active apical tuberculosis and calcification in one kidney, with recurrent hematuria. This kidney was assumed to be tuberculous. Another adolescent, at the age of 15, whose knee had been solidly ankylosed for five years and gave absolutely no evidence of inflammation, was suffering from minimal active pulmonary tuberculosis.

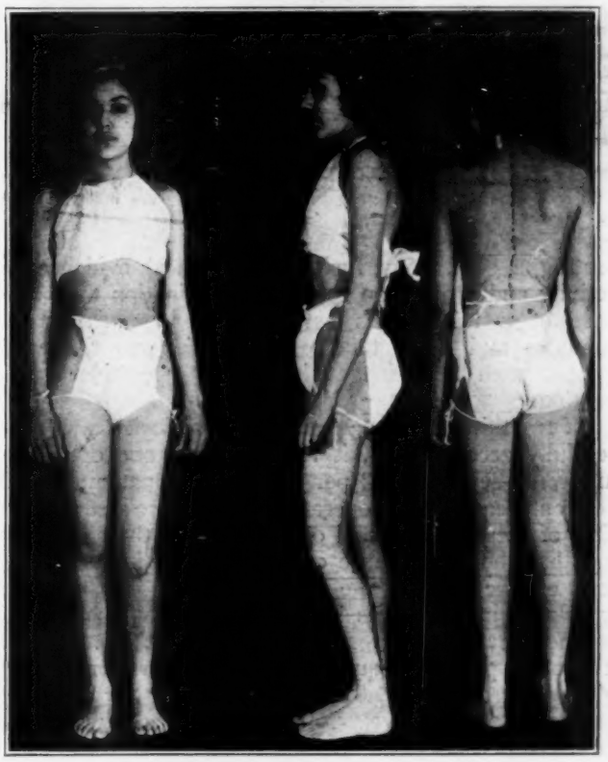

Fig. 4.—The patient whose roentgenogram is shown in figure 3 at the age of 15 with the leg 3.8 cm. short.

These instances of reactivation of pulmonary foci are in keeping with the idea of phthisiologists that late adolescence is a dangerous period. A child of 10 whose ankylosed knee was the site of draining tuberculous osteomyelitis was undernourished but had no other demonstrable tuberculous lesions. None had come to amputation. None had had any other joints involved.

STATUS OF THE KNEE JOINT

Thirty-three, or 97 per cent, of the resected knee joints were solid clinically and by roentgen examination showed trabeculae bridging from the femur to the tibia. One knee exhibited a definite pseudarthrosis by roentgenogram and presented a few degrees of motion after the initial operation. Another knee, although presenting a solid bony fusion, had clinical evidence of activity and showed on roentgen examination the presence of a tuberculous osteomyelitis in the femoral condyles and tibial tuberosities. This was the only patient with a drainage sinus after operative intervention.

Fig. 5.—Resection had been performed thirteen years before, at the age of 4 years.

Of the thirty-three patients in whom fusion was successfully accomplished, it resulted after one operation in twenty-seven, or 82 per cent. Three patients, or 9 per cent, required two operations to produce arthrodesis. One of these was a child operated on at the age of 17 months who had a large caseous abscess in the upper end of the tibia. The operation did not produce ankylosis, but this was successfully accomplished at a second operation, performed in the patient's tenth year. The other patients requiring a second operation were a girl operated on first at the age of 5 and a boy operated on at the age of 4½ years. In neither instance was there any specific reason for the failure of the first operation to result in a fusion.

In two cases, or 6.0 per cent, three operations were required to ankylose the knee. In both the failure was due in the first operation to faulty apposition and in the second to an incomplete procedure. The initial resection was carried out in one instance at the age of 3½ years and in the other at the age of 7 years.

In one case, in which four operations were required before a fusion was accomplished, the first attempt was made at the age of 5. The difficulty was plainly due to very destructive disease. Although the knee joint was eventually ankylosed, tuberculous osteomyelitis with draining sinuses still persists.

Two patients were operated on at the time the knee presented draining sinuses of long duration; in each case fusion resulted from the first operation with no complications.

Thus it appears that with tuberculosis of the knee in infants and children the chance that fusion will result from a single operation is as favorable as it is with tuberculosis in any other joint at any age, and possibly more so.

SHORTENING OF THE EXTREMITY

In determining the amount of shortening, teleoroentgenograms were obtained of all patients. The condition of the epiphysial lines was studied by a comparison of roentgenograms of the arthrodesed knee with similar views of the normal knee. In the classification of the resulting degrees of shortening, the condition of the epiphysial lines was taken into consideration if the age of epiphysial closure had not been reached.

Interrogation of the patients revealed that none wore a shoe elevation adequate to compensate entirely for the actual shortening. Many had tried to but after years of experimentation found that with the stiff knee their gait was more comfortable and appeared more nearly normal with a shoe elevation which failed to compensate for the actual shortening by from 2 to 4 cm.

In the qualification of the results as far as disturbances in longitudinal growth were concerned, all patients who had not yet reached the age of epiphysial closure and whose epiphysial lines showed evidence of departure from the normal were classified as having "severe shortening," even though at the time of examination their actual shortening was less than 5 cm. Patients in whom the epiphysial lines were normal and who had 5 cm. or less of shortening were classified as showing good results in this regard.

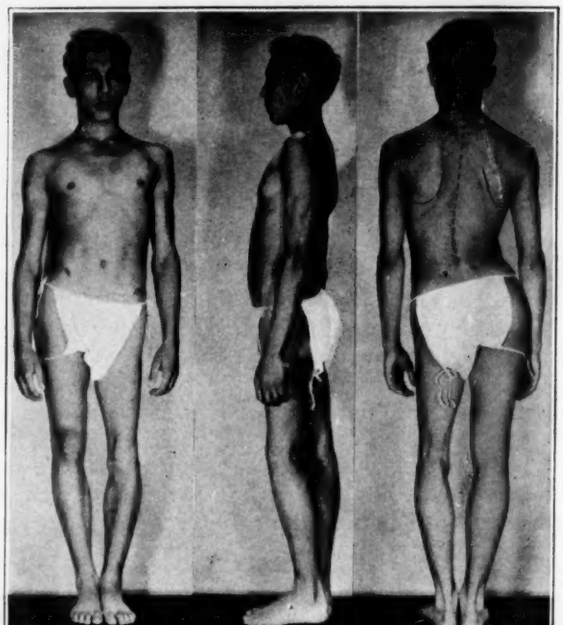

Fig. 6.—The patient whose roentgenogram is shown in figure 4 at the age of 17 with the leg 6 cm. short.

In one case, or 3.0 per cent, the arthrodesed leg was 2.5 cm. longer than the normal leg. The child was, however, only 8 years of age, and the interval since operation had been only one and a half years. Although the

epiphysial lines were normal, it is probable that the ultimate result will be a slightly shortened leg.

In thirty-two cases the average shortening of the surgically treated leg was 4.4 cm. The most severely shortened extremity was that of a 16 year old boy who had been subjected to resection nine years previously, at the age of 7. The diseased leg was 12 cm. (5 inches)

TABLE 1.—*Disturbances of Longitudinal Growth*

Case	Age, Yr.	Interval Since Resection, Yr.	Difference, Cm.	Epiphysial Lines
Lengthening				
1. F. G.	7½	1½	2.5	Normal
Severe Shortening				
1. R. C.	16	9	12	Closed
2. D. M.	10	5	10.5	Destroyed
3. D. M.	12	5	10.0	Closed bilaterally
4. A. W.	20	10	9.5	Closed bilaterally
5. C. C.	8½	3½	8.2	Markedly disturbed
6. F. V.	16	6	7.0	Markedly disturbed
7. M. P.	15	5	6.5	Moderately disturbed (epiphysial arrests on well leg)
8. J. C.	6½	3	6.4	Moderately disturbed
9. F. C.	17	13	6.0	Hazy bilaterally
10. J. R.	9½	4	4.7	Partially disturbed
Negligible Shortening (5 Cm. or Less)				
1. A. V.	21	11	5.0	Closed bilaterally
2. L. R.	12	5½	5.0	Normal
3. H. M.	16	13	5	Hazy bilaterally
4. R. A.	17	13	5.0	Hazy bilaterally
5. M. P.	14	5	4.4	Normal
6. K. S.	19	13	4.0	Closed bilaterally
7. F. M.	20	10	4.0	Closed
8. A. A.	15½	5½	3.8	Normal
9. V. M.	20	13	3.0	Closed bilaterally
10. J. A.	8	4½	3.0	Inner half of tibia disturbed slightly
11. Y. R.	10	3	3.0	Normal
12. M. M.	14	8	2.9	Normal
13. E. A.	13	4	2.5	Normal
14. B. J.	11	5	2.0	Normal
15. F. M.	13	8	1.6	Normal
16. V. R.	5	2	1.5	Normal
17. D. R.	10½	3	1.0	Normal
18. I. D.	4½	1½	1.0	Normal
19. C. A.	12	6	0.8	Normal
20. P. A.	13	5	0.6	Normal
21. E. R.	11	5½	0.5	Normal
22. B. D.	10	3	0.2	Normal

short. The same patient had had a 55 degree genu recurvatum corrected at the age of 13. This deformity had partially recurred. He walked well with a 7 cm. elevation on the heel and sole of his shoe.

Ten patients in all, or 30.3 per cent, of those subjected to resection showed severe shortening or else the condition of their epiphyses indicated that shortening out of proportion to a satisfactory leg was to be anticipated.

Two of these patients had suffered definite injuries to the epiphyses prior to the operation of resection. In a 12 year old boy who showed a 10 cm. shortening five years after fusion of the knee, the lower femoral epiphyses had been dislocated and severely crushed by a manipulation to correct a flexion deformity. In a 15 year old girl, in whom the inequality of the legs had been held down to 6.5 cm. by epiphysial arrests on the normal leg, both the femoral and the tibial epiphyses had been badly damaged by an attempt at extra-articular arthrodesis which was done before the resection.

Three other children, who showed shortening of 10.5 cm., 5 cm. and 6.5 cm., respectively, and who, because of their remoteness from adult bone age and the condition of their epiphyses, were expected to have further shortening, demonstrated the progress of very active disease in which there is extensive caseation of bone. In one case four operations were necessary to produce femorotibial continuity, and even after fusion the knee continued to drain. In another, two resection operations were necessary to produce ankylosis. In the third, although arthrodesis was accomplished in one operation, there had been a large caseous abscess in the upper end of the tibia prior to resection, which had destroyed part of the epiphysial line.

A 16 year old boy who had undergone fusion at the age of 10 years showed 7 cm. of shortening. At the time of fusion his femoral epiphysis was already partially closed by the disease. Further shortening was not anticipated.

An 8 year old child who was first operated on at the age of 5 exhibited 8 cm. of shortening and was expected to show more as the outer half of the femoral and the inner half of the tibial epiphysis were closed. This child was the victim of poor surgical intervention; at the first resection only slight apposition of the femur and tibia was obtained, and three operations were required before bony fusion was obtained.

In three patients, who were subjected to resection at the age of 4, 7 and 8½ years, respectively, there was more than 5 cm. of difference in the length of the legs. A 17 year old boy thirteen years after resection had a leg 6 cm. short. A 16 year old boy nine years after ankylosis had 12 cm. of shortening in the treated leg. A 20 year old girl thirteen years subsequent to resection showed one leg 9.5 cm. short. Bony ankylosis in all these patients resulted after a single operation, and no explanation of this discrepancy other than the result of the operation was evident. Epiphysial arrest was not employed on the well leg in these patients or the distressing disproportion might have been avoided.

Twenty-three patients, or 70 per cent of those subjected to resection, exhibited shortening of less than 5 cm. and had epiphysial lines which were comparable in clarity to the epiphysial lines about the normal knee. Ten of these twenty-three patients had shortening of less than 2.5 cm.

TABLE 2.—*Directional Aberrations*

Case	Age, Yr.	Time Since Resection, Yr.	Flexion	Recurvatum	Valgus	Varus	Torsion	Osteotomy
1. M. P.	15	5	60°	...	...	...	...	Age 12
2. A. W.	20	10	45°	...	...	...	...	Not desired
3. J. C.	6½	3	45°	...	20°	...	...	Age 6
4. L. R.	12	5½	45°	...	...	...	...	Will be necessary
5. F. V.	16	6	40°	...	...	15°	10°	Will be necessary
6. B. J.	11	4½	35°	...	...	...	...	Not desired
7. B. D.	10	3	30°	...	5°	...	...	0
8. R. C.	16	9	...	55°	...	...	...	Age 13
9. V. M.	20	13	...	20°	...	...	...	Age 17
10. E. A.	13	4	...	20°	...	...	...	Age 12
11. J. R.	9½	4½	20°	...	40°	...	...	Age 9
12. C. C.	8½	3½	...	...	20°	...	...	Will be necessary
13. F. A.	13	5	15°	...	10°	...	...	0
14. C. A.	12	6	15°	...	10°	...	...	0
15. M. M.	14	8	10°	...	...	20°	25°	Not desired
16. D. M.	10	5	10°	...	...	12°	5°	0
17. J. A.	8	4½	20°	...	...	10°	10°	Will be necessary
18. F. C.	17	13	15°	...	...	10°	...	0

From these figures it would not seem that the danger of extreme shortening is a legitimate objection to the procedure of economical resection of the knee in children. If the operation is carried out early, the timely application of epiphysial arrests to the well leg when the epiphyses of the diseased leg are badly damaged should hold the disproportion within reasonable limits. In the majority of children this additional surgical intervention to insure against too great a disproportion will not be necessary.

DIRECTIONAL ABERRATION OF THE EXTREMITY

The directional aberrations of growth occurring after the operation of economical resection were, in the order of their frequency, (1) flexion deformity, (2) genu valgum, (3) genu varum, (4) torsion of the tibia on the femur and (5) genu recurvatum. These occurred sometimes singly and sometimes in combination, the most frequent combination being flexion and genu varum.

Flexion of the knee of less than 25 degrees did not seem to be disadvantageous to the patient and was not tabulated as a deformity.

Flexion of more than 25 degrees resulted in seven cases. The most marked flexion deformity occurred in a case in which resection was done at the age of 9 and the epiphysis had been injured by a prior attempt at extra-articular arthrodesis. This deformity, of 60 degrees, was easily corrected by osteotomy at the age of 12. The leg has remained well alined, although slight flexion has recurred since the correction. Three patients had a flexion deformity of 45 degrees. One of these, a girl of 20, who worked as a secretary, did not desire the leg straightened. The extremity of a 6½ year old patient was corrected by an osteotomy, and at a later date another osteotomy will in all probability be necessary, as his epiphyses are seriously damaged by disease. The third, a boy of 12, will probably desire a corrective procedure in the next three years.

A 16 year old patient whose knee had been solidly arthrodesed for six years presented 40 degrees of flexion in combination with moderate varus and torsion and should have the extremity revised. Prior to resection a portion of the tibial epiphysis had been destroyed by tuberculosis. Two other children, aged 10 and 11 years, presented deformities of 30 and 35 degrees. They may need osteotomies in later years, but as they are both girls this is doubtful.

The flexion deformities which resulted in these cases seemed to progress rapidly in the first two years after operation despite adequate immobilization and usually reached their maximum in this period.

A genu valgum deformity occurred in six patients. In one, a child of 9½ years of age, it reached the extent of 40 degrees. In this patient disease had continued to destroy the lateral portion of the femoral epiphysis after the initial resection, and three operations were necessary to produce ankylosis. In another child 20 degrees of valgus was present, with 45 degrees of flexion and 6.5 cm. of shortening. These aberrations were corrected by supracondylar osteotomy. One other child has a knock knee deformity of 20 degrees and will require an osteotomy, as she still has seven years to grow. The three remaining valgus deformities are very mild, two being of 10 degrees and one of 5 degrees, and probably will not require revision.

Five patients exhibited a varus deviation. The greatest bow leg deformity was of 20 degrees in a 14 year old girl. It was associated with internal torsion of the tibia on the femur so that in walking the foot pointed inward about 25 degrees. The patient did not wish it corrected. The four other bow leg deformities were of 15, 12, 10 and 10 degrees, and except for one did not annoy the patient. In this instance the bowing was associated with 40 degrees of flexion.

Internal torsion of the tibia on the femur was present in four cases, but in only one was it of any consequence. Torsion was usually associated with genu varum.

Genu recurvatum occurred three times. In one patient it reached 55 degrees and presented a very unsightly deformity. In two other patients the angle of hyperextension was 20 degrees. All desired relief from the deformity, and all had it corrected by osteotomy. A correction carried out in a girl at the age of 17 had remained perfectly corrected three years later. Two other patients, operated on at the age of 12 and 13, had suffered a slight recurrence of the deformity.

The extremities of seventeen patients had flexion within the optimum of 25 degrees and presented no evidence of varus, valgus or torsion. Five other patients had extremities which showed flexion within the optimum angle but presented a very slight variation in valgus or varus which neither disfigured nor interfered at all with function. These legs will not require osteotomy.

Six patients had had an osteotomy to alleviate a troublesome deformity. Four more patients will probably require correction by osteotomy at a later date and two patients will probably need a second osteotomy.

Of the patients, 66⅔ per cent had no appreciable directional aberration of the extremity; 18.2 per cent had deformities requiring a corrective osteotomy; 15.1 per cent will probably desire an osteotomy to correct a deformity, and two, or 6.0 per cent, who have already undergone one revision may require a second osteotomy because of recurrence of the deformity due to the poor condition of the epiphyses.

On all patients on whom osteotomy had been carried out the operation was done above or below the ankylosed joint. In none was there any reactivation of the tuberculosis.

SUMMARY

For forty-seven patients in the first ten years of life suffering from proved tuberculosis of the knee joint, the most frequent age of onset was found to be within the first four years.

Fifteen patients, or 31.9 per cent, presented a bone abscess in the metaphysial or epiphysial region of the tibia or the femur early in the disease.

One patient remained well, with a normal knee joint, for eight years after extra-articular excochleation of an osseous focus. In five other patients this procedure failed.

Conservative treatment, or surgical procedures short of economical resection, accomplished no satisfactory results in the remaining forty-six patients.

Economical resection healed the tuberculosis in thirty-two of thirty-four patients, or 94.1 per cent, whom it was possible to follow for from one and a half to thirteen years.

The knee joint of a child ankyloses very readily after resection, and the percentage of successful fusions resulting from a single operation is as high as that for ankylosing operations on any other joint.

Extreme shortening after economical resection in infancy and childhood is not the rule; any marked degree occurred in only 30 per cent of the patients. In these it usually resulted from causes extraneous to the resection.

Severe aberrations of directional growth were associated in most instances with previous damage to the epiphyses. They occurred in only 33⅓ per cent of the patients. Moreover, in these they were readily correctable by osteotomy.

CONCLUSION

From this evidence it seems reasonable to conclude that economical resection of the knee is not contraindicated prior to epiphysial closure. Therefore this

procedure should not be withheld until the age of 15 from children suffering from tuberculosis of the knee joint. Rather it should be practiced early after a period of conservative treatment adequate to cause an abatement of signs and symptoms of acute disease.

ABSTRACT OF DISCUSSION

DR. W. P. BLOUNT, Milwaukee: Dr. McKeever has given a convincing argument in favor of arthrodesis or resection of tuberculous knees of older children. The 20 per cent of his cases in which reoperation was required encourage those of us who have had the same experience of failure of fusion at the first operation. He has reopened a subject which has been controversial for years. The proponents of the conservative method of treatment, notably Rollier and men in various European clinics, held that arthrodesis of the knee was never necessary. Ten years ago Rollier was advocating conservative treatment, but I know that a surgeon on his staff was doing arthrodeses in selected cases. Perhaps he has come by now to arthrodesis of the knee in children also. There is no argument in this country as to whether or not this procedure is indicated in older children. The earlier claims of success with conservative methods were artificially colored by the inclusion of nontuberculous knees. On the other hand, the proponents of fusion in infancy are equally incredible. I have had no hesitancy in arthrodesing knees in children over 8 years of age. I prefer to wait a little longer if there is no clearcut indication for early fusion. Most men will agree with this, and the real question is what to do with the very young children with tuberculous knees. It is interesting that in 55 per cent of Dr. McKeever's cases the disease was present before the age of 4. At Milwaukee Children's Hospital I found that in most of the cases the disease was evident before 3 and that half of the children were less than 3 years old at the time they came in for treatment.

DR. R. B. OSGOOD, Boston: I know very little about tuberculosis of the knee. It is a disappearing disease in New England. The tendency, perhaps not the rule, with us has been to delay any attempts at fusion, if we thought it was indicated, until the age of 5 years. With us growth deformity and shortening have not been a negligible factor. Dr. McKeever's paper is very convincing as to the value of arthrodesis from the medical, economic and social point of view, but excessive shortening and very definite operative growth deformities have occurred in his cases in something over 31 per cent, in 11 per cent operative and 20 per cent more in which he expects to operate, and the story is not finished. Surgical intervention has been necessary in about 26 per cent in extreme shortening, and then a stiff knee, after all, is a stiff knee, isn't it, and perhaps the better—but not the best of a bad bargain. When the articular cartilage is beyond repair or is evidently eroded enough so that we know a normal joint will never exist, I think we agree that our better bargain is an arthrodesis procedure. I have nothing to say against the method and I wish to compliment Dr. McKeever on his very careful and thorough and entirely judicial analysis, but I wish to remind you that in the Bible there is something about God promising to save Sodom and Gomorrah if there were—I have forgotten how many—righteous people there. Ten, we will say. They were not found, and Sodom and Gomorrah were destroyed. If we could save a few knees under favorable conditions of tuberculosis in children it would perhaps be worth while to do so. I have seen comparatively few cases of tuberculosis of the knee in early childhood, and I myself have seen only three cases of proved tuberculosis in which apparent recovery has occurred without operation for at least eight years. I can say that in these cases I have had very good luck in having recovery apparently occur with good degrees of motion, by trying to overcome atrophy without allowing the trauma of weight bearing.

DR. HALFORD HALLOCK, New York: Our experience at the New York Orthopedic Hospital has been very much the same as Dr. McKeever's. In 1915 we gave up treating tuberculosis of the knee by conservative methods because we could not obtain cures and began using fusion. Since that time our series has run to 200 or 300 cases, about 70 per cent of which have been proved to be tuberculous. Over 90 per cent became fused by the first operation. The knee joint is one of the easier ones to fuse and we have had but little trouble in obtaining arthresis. We have also had some trouble with shortening. I should say that perhaps 10 or 15 per cent of our cases have ended with considerable shortening, as in Dr. McKeever's 30 per cent. We believe that the probable cause was the fact that operation was delayed too long. The disease had already produced disturbances or destruction of the epiphysial lines before fusion was performed. We feel that, in order to prevent all this shortening, arthrodesis must be done before the disease has partially or completely destroyed the epiphysial lines. I should like to say something about deformities in the younger children. It is our custom in children to fuse the knees at 180 degrees, because we have found that otherwise flexion deformities may occur through the distal epiphysial line of the femur. We also use braces for a number of years after fusion in very young children in order to prevent slipping through this epiphysial area. I should like to ask whether Dr. McKeever has fused the knee joint of all his younger patients in from 10 to 25 degrees of flexion. I still believe that tuberculosis of the knee should be operated on even at an early age and that fusion is the only method which will give a large percentage of cures in these cases. So far I have never seen a recurrence of tuberculosis in a knee that became fused and that has been since 1915.

DR. FRANK R. OBER, Boston: There are some cases of tuberculosis of the knee in which complete recovery occurs without any operation, but these are the cases in which the tuberculous process does not go into the knee joint. It does not extend through the epiphysis but does extend laterally and decompresses itself through the side of the bone, either laterally or medially. In such cases healing takes place without any disturbance to the knee joint whatever and fusion should not be done on such patients. Dr. McKeever had six cases of forty-nine which showed no fusion after one or more operations. At the New England Peabody Home, where we have a large number of children affected with bone and joint tuberculosis, we feel that unsuccessful fusions are not always the result of faulty technic but are often due to other conditions which result from a general tuberculous process. All of these cases are studied thoroughly by a pediatrician. Roentgenograms of the chest are taken and if there is any sign of active pulmonary lesions we believe that operation on a tuberculous joint is contraindicated. Furthermore, if the child has a high monocyte count and a low lymphocyte count and fusion is done, the fusion tends to melt down and there is a recurrence. This monocyte-lymphocyte ratio, when high, shows that there is too much activity of the tuberculous process and we have learned not to operate until the ratio is normal.

DR. FRANCIS M. MCKEEVER, Los Angeles: In answer to the question about the position in which these knees were placed postoperatively, most of them were placed within 10 degrees of a straight angle. Arthrodesing a tuberculous knee in a child is not, of course, the ideal procedure; however, as in some questions of government and also in medicine, it is a question of the lesser of two evils and I believe that this procedure is better than going on with the malady. In our experience the tuberculous knees in children have not done as well as they have in New England.

What Constitutes Normality?—Medical men are insufficiently conversant with what constitutes normality, or the range of normality, in the human being. They regard as pathological many phenomena which are in reality not only compatible with health, but are actually physiological. It is of much consequence that this argument should be brought home. . . . Take a very simple case: Stroke the back of a normal healthy young subject and watch the vascular reaction in the skin; the line pressed and the surrounding skin displays after a while a red line; maybe it soon becomes surrounded by an area of blanching, maybe a line of blanching alone appears. These reactions, perfectly healthy reactions as they are, have been used, are still used, and will be used for many years to come, as important signs of particular and serious disease.—Lewis, Sir Thomas: Research in Medicine and Other Addresses, London, H. K. Lewis & Co., Ltd., 1939.

HYPOTHYROIDISM IN THE CAUSATION OF ABORTION, ESPECIALLY OF THE "MISSED" VARIETY

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Whether we are entirely correct in applying the term "hypothyroidism" in each of the cases under consideration might be questioned, as the diagnosis is based chiefly on the determination of the basal metabolic rate. However, as we are concerned particularly with early pregnancy, in which indefinite manifestations such as malaise and fatigability are so common, we find that we are not in a position to base our diagnosis on the usual symptoms of hypothyroidism. It is our opinion, moreover, that the minor degrees of this state may be practically symptomless and yet may seriously affect the reproductive function. This is in accord with the views of Litzenberg and Carey,[1] who stated that "it would seem apparent that any deviation from the normal rate must be due to thyroid influence and

TABLE 1.—*The Thyroid in Relation to Abortion*

	No. of Women	Abortions	
		Previous	Present
Hyperthyroid	17	3	1
Normal	72	4	1
Hypothyroid	61	13	8
	150	20	10

TABLE 2.—*Abortions in the Hyperthyroid Group*

Primiparas	12
Multiparas	5
Abortions previously	3
Abortions in present series	1

inasmuch as the patient usually responds to thyroid medication we have used the term 'hypothyroidism' in spite of the fact that clinicians in general seem reluctant to attach a diagnosis of hypothyroidism to a patient with low basal metabolic rate." However, as Litzenberg[2] later stated in Curtis's system, other endocrine factors may be involved in some patients with low basal metabolic rates. It is difficult, if not impossible, to segregate such patients from those in whom the abnormality is of thyroid origin; we feel, moreover, that the number of such patients is small and hence that it is proper to group all patients with low basal metabolic rates together.

A considerable amount of investigation has been conducted in the field of the basal metabolism of pregnant women, but emphasis has been placed chiefly on the latter half of pregnancy. Only a few reports of determinations of the basal metabolism in early pregnancy are to be found in the literature. The consensus is that in normal gestation the basal metabolic rate is little altered in the early months and steadily rises as pregnancy advances, reaching, according to Baer[3] and Cornell,[4] a level from 25 to 35 per cent above normal at term.[5] The Roots[6] state that the rise in the rate is out of all proportion to the increase in the maternal weight. Sandiford and Wheeler[7] hold that the altered production of energy in the latter part of pregnancy is due to the increased mass of active protoplasmic tissue, chiefly fetal, and not to a change in the amount of heat produced per unit volume of maternal tissue. This opinion has been reaffirmed in a later paper.[8] Du Bois[9] states that the metabolism averages —8 per cent early in pregnancy and mounts in a straight line to +7 per cent just before delivery (quoting the results reported by Rowe, Alcott and Mortimer[10]).

It is apparent, then, that one should expect approximately normal basal metabolic rates early in pregnancy and that the same criteria as to what may be considered abnormal rates are to be observed. Litzenberg and Carey[1] class obstetric patients with rates of — 10 or below as hypothyroid. Sloan,[11] writing of hypothyroidism in general, feels that there are many persons with rates of — 10 or even less and other mild suggestive signs and symptoms who should be classed as hypothyroid. Sterility in women with hypothyroidism was first mentioned by Litzenberg,[12] and his observation has been abundantly confirmed by many other authors.

The association of a low metabolic rate in early pregnancy with an increased tendency to abortion has been noted by several writers. Litzenberg and Carey[1] report that of seventy-eight married women with a low basal rate thirty-five (or 45 per cent) were absolutely sterile, six had had abortions or stillbirths (but no living children), and nine with one or more living children had also had one or more abortions or stillbirths. Besides, they found that seventeen (or 30 per cent) of fifty-two sterile women with a low basal metabolic rate conceived after treatment with thyroid extract; two of these aborted because they discontinued treatment after conception had occurred. These authors feel that a normal metabolic rate should be maintained during pregnancy. Huntington[13] reported a case in which there had been three pregnancies at term and then three abortions; the patient was then found to have a basal metabolic rate of —21. Another patient had had an abortion, then a full term pregnancy and then another abortion one year later, at which time the rate was —17. Abruzzese[14]

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found that of thirty aborting women five had a low basal metabolic rate and eleven an abnormally high rate. Taussig [15] states that if the rate is between —10 and —30 thyroid extract should be given and will often prove to be a factor in the prevention of abortion. However, it does not appear that the importance of hypothyroidism as a factor in the causation of fetal death and subsequent abortion has been sufficiently stressed in medical literature; hence we feel that a presentation of our experience may be of interest.

This report represents a study of the basal metabolic rate of 150 pregnant women, all private patients. The readings were taken in the early months of pregnancy except in two cases, in which it was first taken after miscarriage had occurred. The association of abortion with rather marked hypothyroidism had previously been noted in several instances. We began to determine the basal metabolic rate in all cases of early pregnancy except those of multiparas with clear records, and we have recently decided to include them as well. We have not made it a practice to make determinations for women first consulting us in the latter half of pregnancy, as it appears that any interference with gestation ascribable to the thyroid deficiency will practically always develop during the first four months. It might be advisable to test these patients as well; in one patient seen in consultation near the end of pregnancy the intra-uterine fetal death could be ascribed only to hypothyroidism, the rate being —16.

Of these 150 women, seventeen were found to be hyperthyroid (basal metabolic rate +10 or over), seventy-two had normal readings and sixty-one (or 40.6 per cent) were hypothyroid. Of the seventeen in the first group, five were multiparas; three of these had aborted in a previous pregnancy. One of these hyperthyroid patients aborted while under our observation. Of the seventy-two women with normal rates, ten were multiparas with four previous miscarriages. There was only one abortion in this group of seventy-two; eight threatened abortions were averted. However, the patients with rates between —6 and —9 were given small doses of thyroid extract prophylactically, especially if they had aborted in previous pregnancies. We feel that this was a factor in reducing the number of abortions; it will be noted that there were four previous abortions but only one in the present series of pregnancies. Of the sixty-one women in the hypothyroid group, eleven were multiparas who had had thirteen previous miscarriages. There were eight abortions. Two of the women had been adequately treated, while in six cases the hypothyroidism was not detected promptly because the patient was not seen sufficiently early, there was little or no treatment and abortion occurred. For the other patients of this group the diagnosis was made early, treatment with thyroid extract was instituted promptly and the pregnancy went to term. There were eleven cases of threatened abortion. We feel that the fetal loss would otherwise have been much greater, especially since in some instances the rate was as low as —20 to —23.

Some of these hypothyroid patients presented clinical experiences which seem to us to substantiate our contentions very definitely. One woman had had a thyroidectomy at 17. Her first pregnancy resulted in intra-uterine fetal death and miscarriage at the sixth month. The next baby was carried to term and born alive; the mother took thyroid extract regularly during this pregnancy. After this she was extremely remiss regarding treatment, and the basal metabolic rate varied between —16 and —22 on the rare occasions when she reported for examination. Since this term pregnancy in 1934, she has had three spontaneous miscarriages at from two to three months, all due, we are sure, to her failure to continue systematic and adequate thyroid dosage. Another patient was first seen at two and one-half months. A threatened miscarriage developed a few days later but abortion was averted. The basal metabolic rate was —10; thyroid extract was administered and she went to term. The administration of thyroid extract was discontinued and nine months later she aborted at six weeks (there was no embryo in the intact sac); the basal metabolic rate was —12. The thyroid treatment was continued. She became pregnant again five months later and was delivered at term. Another patient, after being delivered at term in 1927, has had eight spontaneous abortions at from two and one-half to three months' gestation. Her basal metabolic rate in May 1937 was —13, while that of her husband was —6. They have not been seen since that date. A fourth woman miscarried at five months in 1925, delivered at term in 1926, miscarried at six months in 1934 and aborted at between six and eight weeks in 1935. In June 1936 she became pregnant again and was first seen by one of us in September, at which time the basal metabolic rate was —17. Thyroid extract 2 grains (0.13 Gm.) a day was administered and she was delivered of a living child at term.

TABLE 3.—*Abortions in the Normal Group*

Primiparas	62
Multiparas	10
Abortions previously	4
Abortions in present series	1
Abortions, threatened, in present series	8

TABLE 4.—*Abortions in the Hypothyroid Group*

Primiparas	50
Multiparas	11
Abortions previously	13
Abortions in present series (Only two in women adequately treated)	8
Threatened abortions	11

The term "missed abortion" refers to the retention of the intact products of conception in the uterus for a considerable period after death of the ovum. There is some difference of opinion as to the length of this time interval. Litzenberg placed it at two months or more, while Streeter (quoted by Taussig [15]) believes that from four to six weeks usually elapses between the death of the fetus and its expulsion. Taussig [16] believes that all cases in which the complete ovisac is retained after death of the fetus or embryo should be included under this classification. Hence the reported frequency of this condition will vary according to the varying ideas of the authors as to the precise definition of the term. We are inclined to agree with Taussig that no hard and fast rule can be adopted; however, the fetal death will usually have occurred from six to eight weeks before the diagnosis is definitely made or the mass is expelled. In this series there were three previous missed abortions and three in patients under our

15. Taussig, F. L.: Abortions Spontaneously Induced, St. Louis, C. V. Mosby Company, 1936, p. 104.

16. Taussig,[15] p. 246.

observation. In addition there were two women (one the thyroidectomized patient before mentioned) in whom fetal death occurred rather late, at the sixth month and at the eighth. Both women were noticeably hypothyroid clinically and their rates varied between —16 and —25. We therefore feel justified in considering the hypothyroid state an important etiologic factor in the missed abortion.

We believe that hypothyroidism is of rather frequent occurrence in our section of the country and that its frequency is therefore increased in pregnancy as well. Mahorner [17] is of the same opinion and informs us that this condition is more common with us than in some other localities. We shall not attempt to theorize as to the factors which might be responsible.

We feel justified in concluding, therefore, that hypothyroidism of mild or moderate degree is a fairly common complication of pregnancy. The severer types, particularly when associated with the same condition in the husband, will be found to be productive of sterility. It therefore appears logical to determine the basal metabolic rate as a routine in early pregnancy and to institute proper treatment when the rate is found to be low. We believe that by so doing we have been able to carry many patients to term who might otherwise have aborted because of the hypothyroidism.

SUMMARY OF THREE ILLUSTRATIVE CASES

CASE 1.—Mrs. B. had had a thyroidectomy at 17. In her first pregnancy, intra-uterine fetal death occurred at the sixth month. In her second pregnancy she was treated with thyroid, and she was delivered at term. In the third, fourth and fifth pregnancies she had little or no treatment; the basal metabolic rate varied from —17 to —22 and all terminated in miscarriage.

CASE 2.—In the first pregnancy there was a threatened miscarriage; the basal metabolic rate was —10, and delivery took place at term. The second pregnancy ended in abortion at the sixth week; there had been no treatment, and the basal metabolic rate was —12. During the third pregnancy the patient was treated and she was delivered at term.

CASE 3.—A delivery at term took place in 1929, and there have been eight miscarriages since. The wife's basal metabolic rate was —12 and the husband's —9.6.

ABSTRACT OF DISCUSSION

DR. J. C. LITZENBERG, Minneapolis: Moll asked his students when they went out into practice to send him the products of abortion so that he could study them embryologically. He determined the age of the ovum by embryologic methods without a knowledge of the menstrual history. He first determined the embryologic age and then, by the case history, the menstrual age. He found that the embryologic age and the menstrual age were six weeks apart; that the embryo or fetus was generally six weeks younger than the menstrual age would indicate. Hence the fetus had died six weeks before it was aborted. Moll also brought out another important point which has been subsequently elaborated and discussed by Streeter and his colleagues, and that is that most abortions are due to the death of the fetus and that the cause of this death is defective germ plasm. Now defective germ plasm is not a microscopic determination. As Streeter gives the definition, it is not a study of the histologic type or histologic-pathologic conditions in the fetus, but the fetus or embryo, as the result of defective germ plasm, simply does not develop and it dies and an abortion results. The old ideas of trauma and the like are of minor significance. In my first two papers, the second with my colleague Dr. Carey, I found that there is an intimate relation between hypothyroidism or just low basal metabolism (I think we can continue to call it hypothyroidism) and abortion. This relation, as Dr. King has quoted, we found definite in 45 per cent of all of our sterile women, i. e. 45 per cent of them had low basal metabolic rates. The fact to which I wished to call attention at that time was that moderately low rates affected conception and abortion. It was perfectly well known before that time that there was a relation between the thyroid and conception when rates were very low. Women with myxedema seldom conceived. When they conceived they would abort. But the fact to which I called attention was that a basal metabolism of very moderate degree also interfered with conception and caused abortions. There is quite a difference between the relation of basal metabolism to disease and its relation to the physiology of pregnancy. The cells of the gonads are very susceptible to deleterious influences and therefore fusion between an ovum and a sperm either one of which is below par will give an embryo that is below par, the fetus doesn't develop properly, therefore it has defective germ plasm, and it dies and an abortion occurs. We found that 45 per cent of women who were sterile had low basal metabolic rates. Furthermore, we found that 46 and a fraction per cent of all girls who had menstrual disturbances of all kinds—we made no distinction—had low basal rates. We approached the subject from another angle. Then we tried also to find out what percentage of women who had low basal metabolic rates did not conceive. The relation was quite as close, being more than 40 per cent.

DR. JESSE W. WHITE, Pueblo, Colo.: In our community in Colorado there are a great many women with a slightly lowered basal metabolic rate. About 80 per cent of those women will be relieved of the symptoms of fatigue and nervousness by the giving of desiccated thyroid. A number of women were found to be aborting apparently as a result of the hypothyroid condition, and I found also that it was a factor in the slow recovery after pregnancy. Many women who complained of excessive fatigue and inability to do their work at the usual time following delivery could be brought back to normal within a relatively short time by the giving of desiccated thyroid when the metabolic rate was low. Hunt and his associates have recently reported experimental work which shows fairly conclusively, I feel, the relationship of hypothyroidism to toxemias of pregnancy and shows how these abortions may occur. They have shown that with this hypothyroid condition there is an increase in cholesteremia and also marked infarcts in the placenta which apparently are due to endarteritis, probably caused by the high cholesterol content in the blood. It is my opinion that practically all communities have these cases of low metabolic rate with practically no symptoms other than fatigue and sometimes nervousness and that potentially these are women who will abort or be relatively sterile. This condition is not confined to women as far as sterility is concerned, since I have had numbers of cases in which a low metabolic rate in the male was the apparent cause of a childless marriage until after desiccated thyroid had been given.

DR. FRED J. TAUSSIG, St. Louis: The time to start the treatment for the prevention of spontaneous abortion is before conception has occurred. I think if we delay treatment until after conception has occurred we shall often have an ovum that is primarily blighted and nothing that we can do will prevent the unsuccessful termination of the pregnancy at term. Treatment, however, should not be limited to a study of the thyroid function. I think pelvic factors should be taken into consideration and the other endocrine organs be given a careful review. Unfortunately there are relatively few accurate tests to determine the function of sex glands and the pituitary. Physicians depend on the basal metabolism test perhaps too much, but at any rate it is an index of thyroid deficiency, and if we include the husband as well as the wife in the preliminary treatment when there is a relatively low basal metabolism test, we shall often get a successful implantation and a development of the ovum to term. I feel also that vitamin E is a substance that seems, at least in a certain number of cases, to stimulate the development of healthy ova. For that reason, in this preliminary, preconceptional treatment I often give both husband and wife small doses of thyroid if there is a low basal rate, and also put them on a high vitamin E diet.

17. Mahorner, Howard L.: Personal communication to the authors.

CRYSTALLINE INSULIN

ALEXANDER MARBLE, M.D.
AND
ILMARI VARTIAINEN, M.D.
BOSTON

"Crystalline insulin" was released for general sale in August 1938 under the name "insulin specially prepared as solution of zinc insulin crystals." However, in contrast to the other two types of insulin now commercially available, the regular type (amorphous, unmodified) and the protamine zinc insulin, its rapidity of action and duration of effect have remained controversial. In the hope of clarifying the issue, in November 1938 we undertook a comparison of the action of regular insulin (prepared from amorphous material) with that of solution of zinc insulin crystals and now present the results of the study.

In 1926 Abel [1] and his associates succeeded in obtaining insulin in crystalline form from highly purified amorphous preparations. Scott [2] in 1934 noted that samples of such crystalline preparations contained traces of zinc; he observed also that crystals were formed only in the presence of certain heavy metals—zinc, nickel, cobalt or cadmium. By the addition of small amounts of zinc to protamine insulin, prolongation of effect of this already slowly acting preparation was reported by Scott and Fisher; [3] increased duration of action was noted also when relatively large amounts of zinc were added to regular insulin.

Sahyun [4] stated that at p_H 6.0 to 6.6 the solubility in aqueous solution of zinc insulin crystals was substantially less than that of amorphous preparations and suggested that, following subcutaneous injection, the rate of absorption of the crystalline type might be slower and its action longer than that of the amorphous variety. Clinical studies have been carried out by various groups of workers to investigate this point. The results have in most instances [5] been interpreted as indicating that the duration of effect of a solution of zinc insulin crystals is much greater than that of insulin prepared from amorphous material. In one report recently published [6] the authors, although recognizing the longer action of protamine zinc insulin, speak of the crystalline type as a "long acting" insulin and state that "those diabetics transferred to crystalline insulin were better controlled than those on protamine zinc insulin alone or in combination with regular insulin." Some have stated that its length of action on the blood sugar is two or more times as great as that of insulin of amorphous type.[7]

On the other hand, the early studies of Howard and deLawder [8] on four diabetic patients failed to show any appreciable difference in effect between insulin made from crystals (prepared in the department of pharmacology of Johns Hopkins University) and insulin made from amorphous material. From his experience with a preparation of insulin crystals (content of zinc not stated), Wilder [9] concluded that, although its action was longer than that of insulin made from amorphous material, it was not comparable to that of protamine insulin. He stated that the duration of effect of the solution of crystals was not long enough to permit the treatment of severe diabetes with fewer than two injections a day. Myers and Perkin [10] found a marked similarity between the effect of the crystalline and the amorphous types and concluded that there was little, if any, difference in the action of the two types. Sahyun [4b] quotes Myers as stating that more recently he has observed prolongation of action following the use of a solution of zinc insulin crystals. Nelson and Dummer [11] found it impossible to control the blood sugar of children with severe diabetes during the night by the injection of a solution of crystals, either at 5 or at 9 p. m., since almost invariably attempts to control the fasting blood sugar of the following morning resulted in serious hypoglycemic attacks during the night.

Almost without exception, studies in normal animals, such as those of Blatherwick, Ewing and Bradshaw [12] in rats, have failed to show any striking difference between the action of amorphous and crystalline preparations of insulin. It is true that Kohl [13] asserted that in rabbits insulin of the crystalline type exerted a somewhat greater effect than did that of the amorphous type, but in his paper no mention was made of the amount of zinc in the preparations used. Sahyun [14] has recently reported the results of comparative tests on rabbits, using thirty-three animals for each preparation tested; the average blood sugar curves obtained with the two types of insulin were very similar.

MATERIALS

Samples of "insulin specially prepared as solution of zinc insulin crystals" and of insulin prepared from amorphous material of Eli Lilly & Co. and of Frederick Stearns & Co. manufacture were used in the studies. The Lilly products were furnished us by that company

Dr. Vartiainen is the holder of a fellowship of the Finnish government.
Miss Rachel M. Smith and Miss Alison T. Fernald gave technical assistance.
From the George F. Baker Clinic, Elliott P. Joslin, M.D., Medical Director, New England Deaconess Hospital.
The board of the patients, the compensation of the medical students who served as normal subjects, the cost of certain supplies and the salaries of Mrs. Rita M. Reed and Miss Frances Waterhouse, who gave technical assistance during the period of the study, were paid by Eli Lilly & Co. Part of the insulin used was purchased by funds of the United States Food and Drug Administration.

1. Abel, J. J.: Crystalline Insulin, Proc. Nat. Acad. Sc. **12:** 132 (Feb.) 1926.
2. Scott, D. A.: Crystalline Insulin, Biochem. J. **28:** 1592 (Aug.) 1934.
3. Scott, D. A., and Fisher, A. M.: Studies on Insulin with Protamine, J. Pharmacol & Exper. Therap. **58:** 78 (Sept.) 1936.
4. (*a*) Sahyun, Melville: Zinc Insulin Crystals, Detroit Chemist. **10:** 240 (Dec.) 1938; (*b*) Crystalline Insulin, J. M. A. Georgia **28:** 39 (Feb.) 1939.
5. Freund, H. A., and Adler, Sidney: Effects of Standard, Protamine, and Crystalline Insulin on Blood Sugar Levels, J. A. M. A. **107:** 573 (Aug. 22) 1936. Mains, M. P., and McMullen, C. J.: The Clinical Investigation of an Improved Crystalline Insulin, ibid. **107:** 959 (Sept. 19) 1936. Altshuler, S. S., and Leiser, Rudolph: Clinical Experience with an Improved Crystalline Insulin, ibid. **107:** 1626 (Nov. 14) 1936. Feinblatt, H. M., and Ferguson, Edgar: Report of Comparative Blood Sugars in Diabetes with Standard Insulin and with New Improved Insulin, M. Rec. **145:** 67 (Jan. 20) 1937. Barach, J. H.: Experimental Studies on the Effect of Insulin, Protamine Insulin and Crystalline Insulin, Pennsylvania M. J. **40:** 349 (Feb.) 1937. Allen, F. M.: Protamine Insulin and Diabetes Treatment, M. Times **65:** 608 (Dec.) 1937. Altshuler, S. S.: The Clinical Use of Crystalline Insulin, Ann. Int. Med. **11:** 901 (Dec.) 1937. Altshuler, S. S., and Leiser, Rudolph: The Use of Crystalline Insulin in the Treatment of Patients with Severe Diabetes, J. Michigan State M. Soc. **37:** 980 (Nov.) 1938. Shepardson and Friedlander.[6]
6. Shepardson, H. C., and Friedlander, R. D.: Clinical Experiences with Long-Acting Insulin in Ambulatory Diabetic Patients, Ann. Int. Med. **12:** 830 (Dec.) 1938.
7. Bowcock, H. M.: Solution of Zinc-Insulin Crystals—A New Therapeutic Agent, Editorial, J. M. A. Georgia **27:** 361 (Sept.) 1938.
8. Howard, J. E., and deLawder, Agnes: Crystalline Insulin in the Treatment of Diabetes Mellitus, Bull. Johns Hopkins Hosp. **52:** 173 (March) 1933.
9. Wilder, R. M.: Clinical Investigations of Insulin with Prolonged Activity, Ann. Int. Med. **11:** 13 (July) 1937.
10. Myers, G. B., and Perkin, F. S.: Comparative Effects of the New Insulin Preparation upon the Blood Sugar Curve, J. Lab. & Clin. Med. **23:** 1 (Oct.) 1937.
11. Nelson, W. E., and Dummer, Clyde: Clinical Experience with Protamine and Cystalline Insulin in the Treatment of Diabetes Mellitus in Children, J. Pediat. **10:** 446 (April) 1937.
12. Blatherwick, N. R.; Ewing, M. E., and Bradshaw, P. J.: Some Effects of Zinc and Iron Salts on the Hypoglycemic Action of Insulin in Rats, Am. J. Physiol. **121:** 44 (Jan. 1) 1938.
13. Kohl, Hans: Ueber kristallinisches Insulin: VIII. Ueber die Standardisierung des kristallinischen Insulins nach der Flächenwertmethode, Arch. f. exper. Path. u. Pharmakol. **182:** 550, 1936.
14. Sahyun, Melville: Effect of Zinc on Insulin and Its Mechanism, Am. J. Physiol. **125:** 24 (Jan. 1) 1939.

in the form of "unknowns" labeled insulin A and insulin B. Not until the study was completed were we told that insulin A was of the crystalline and B of the amorphous variety. We were assured in writing that both insulins were taken by Eli Lilly & Co. from lots prepared for distribution and actually dispensed

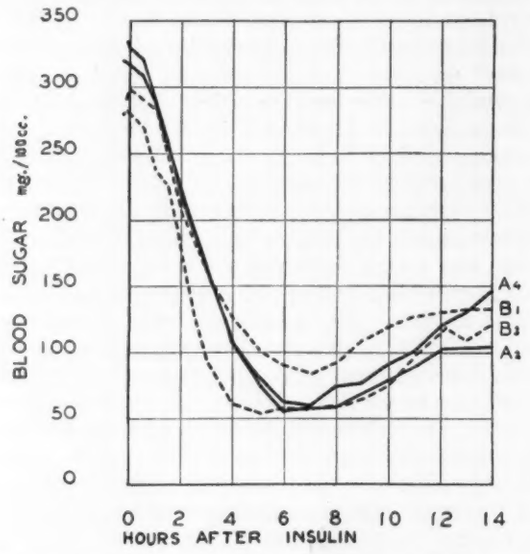

Chart 1 (case 1).—Blood sugar curves following single doses of insulin-Lilly (0.2 unit/Kg.). Food was withheld throughout the tests. B_1, amorphous, Nov. 16, 1938; A_2, crystalline, Nov. 21; B_3, amorphous, November 26; A_4, crystalline, December 1.

E. R., a man, aged 23.5 years, had had diabetes since September 1928. The diet during the period of study was carbohydrate 175 Gm., protein 101 Gm., fat 130 Gm. Body weight, 122 pounds (55.3 Kg.); height, 64 inches (163 cm.).

Note that in this and in the following charts the rapidity of effect of the two types of insulin was essentially the same, as evidenced by the rate of fall of the blood sugar. The two curves B_1 and B_3, showing the effect of the amorphous type, obviously differ very little from the other two curves, which give the results with the solution of zinc insulin crystals. There was, to be sure, a spread of about 50 mg. in the initial values of the four curves. This degree of variation on different test days is difficult to avoid in patients with severe diabetes. We have preferred to present the actual data rather than attempt to adjust the initial values to a uniform starting level.

commercially. The Stearns products were purchased on the open market and delivered to us by inspectors of the Boston office of the United States Food and Drug Administration. All samples used were stated by the manufacturers to contain 40 units per cubic centimeter.

In table 1 are shown the results of the analyses of the preparations used. The values for potency, nitrogen content and zinc content were furnished us by the Insulin Committee of the University of Toronto. Both Frederic Stearns & Co. and Eli Lilly & Co. supplied us with the results of their own determinations of the nitrogen and zinc content of their respective products. The values for nitrogen were in each instance almost identical with those obtained by the Insulin Committee. Those for zinc did not agree quite as closely, but the slight differences are not surprising, since the accurate determination of minute quantities of zinc is difficult; minor discrepancies between figures furnished by different laboratories must be viewed with this in mind.

In addition to the analyses for which results are shown in table 1, biologic assays of the four samples of insulin were carried out in the laboratories of the Insulin Committee, from forty-eight to eighty-two rabbits being used for each comparison. In these studies the effect on the blood sugar of each type of insulin was compared with that of the other type of the same manufacturer and in some instances with that of a preparation of insulin crystals (S-220), which, since the early part of 1936, has been the official standard of reference for insulin supplied in the United States and Canada. The average blood sugar curves obtained showed, in the case of the products of each manufacturer, the effect of the solution of zinc insulin crystals to be almost identical with that of insulin prepared from amorphous material. That similar results have already been reported by Sahyun [14] has been mentioned earlier in this paper.

CHEMICAL METHODS

The blood sugar was determined on capillary samples by the micro procedure of Folin and Malmros.[15] The percentage of sugar in the urine was determined by Smith's [16] modification of Benedict's method. Folin's [17] micro Kjeldahl method for the determination of total nitrogen in the urine was used.

PLAN OF INVESTIGATION

Diabetic Patients.—Eight patients, four men and four women, with diabetes of moderate or severe grade served as subjects. They spent the entire period of study, from thirty-three to seventy-three days, in the hospital under conditions which were controlled as carefully as possible. All were reliable, intelligent and cooperative. Their ages ranged from 20 to 58 years. With one exception all patients had had diabetes for ten or more years; patient 3 had had the condition for 4.8 years. The details regarding individual patients are given in the legends for the various charts.

The plan of investigation was as follows: Each patient was kept on a constant, weighed diet; the

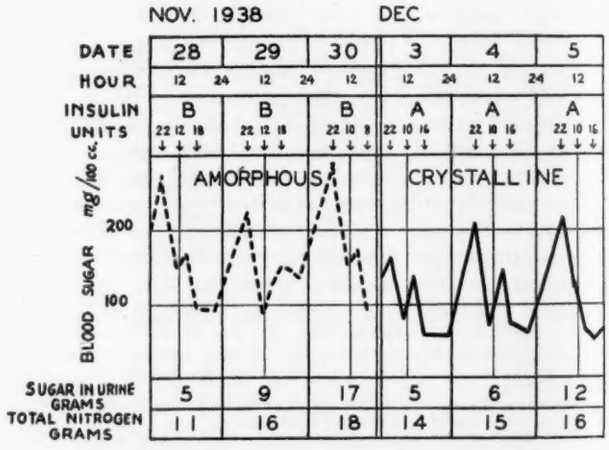

Chart 2 (case 1).—Response to insulin B (Lilly, amorphous type) and insulin A (Lilly, solution of zinc insulin crystals). As in the other charts, the broken line is used for blood sugar curves during days of maintenance on insulin of the amorphous type and the solid lines for those during days of maintenance on the solution of zinc insulin crystals. Insulin was administered at 7 a. m., 12 noon and 5 p. m. daily in the amounts indicated. In the hourly schedule that appears beneath the days of the month, 12 is used to indicate noon and 24 to indicate midnight.

It is evident that with this patient blood sugar values were somewhat lower during the period of maintenance on the solution of zinc insulin crystals. However, despite the fact that sufficient insulin was given before supper to cause low blood sugar values at 10 or 11 p. m., this dose did not prevent a rise of the blood sugar to over 200 mg. per hundred cubic centimeters by 7 a. m. the following morning. Furthermore, it is evident that glycosuria was only slightly less when the crystalline type was used. The average daily excretion of nitrogen in the urine was the same with the two types of insulin.

amount of carbohydrate ranged from 137 to 247 Gm. a day. The quantity of sugar and, in five of the eight patients, the quantity of nitrogen excreted in the urine

15. Folin, Otto, and Malmros, H.: An Improved Form of Folin's Micro Method for Blood Sugar Determinations, J. Biol. Chem. **83**: 115 (July) 1929.

16. Smith, M.: A Micromodification of the Method of Benedict for the Quantitative Determination of Reducing Sugar in Urine, J. Lab. & Clin. Med. **7**: 364 (March) 1922.

17. Folin, Otto: Micro Kjeldahl Colorimetric Method for the Determination of Total Nitrogen in Urine, Laboratory Manual of Biological Chemistry, ed. 5, New York, D. Appleton-Century Company, 1934, p. 145.

in twenty-four hours was determined daily. In addition, qualitative tests for sugar were carried out at 6:30, 9:30 and 11:30 a. m. and at 2:30, 4:30, 7:30 and 9:30 p. m. daily. Determinations of the capillary blood sugar were made at 7 and 11 a. m. and at 2, 5 and 10 p. m. daily throughout the study except on certain

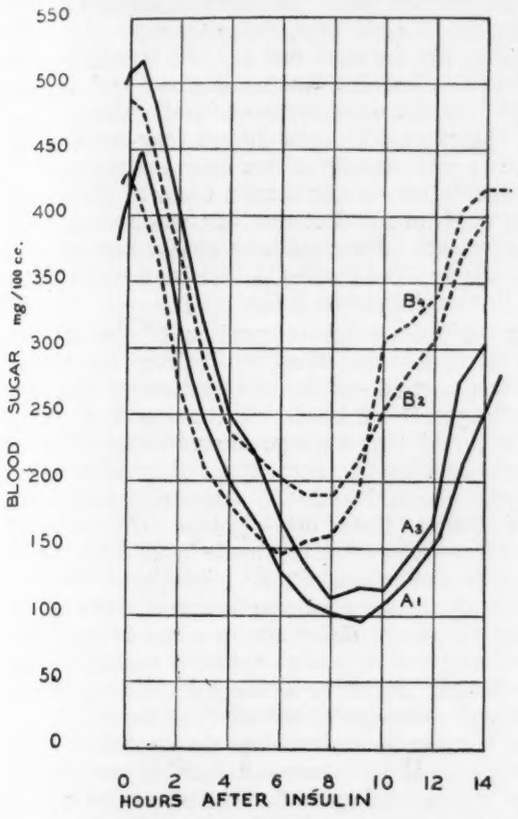

Chart 9 (case 5).—Blood sugar curves following single doses of insulin-Lilly (0.15 unit/Kg.). Food was withheld throughout the tests. A_1, crystalline, Nov. 22, 1938; B_2, amorphous, November 29; A_3, crystalline, December 5; B_4, amorphous, December 10.

Miss E. M., aged 58.4 years, had had diabetes since July 1917. The diet during the period of study was carbohydrate 137 Gm., protein, 79 Gm., fat 98 Gm. Body weight, 120 pounds (54.4 Kg.); height, 65½ inches (166 cm.). The curves in this case were much like those in case 4 shown in chart 7. There is no doubt that the curves A_1 and A_3, obtained with the solution of zinc insulin crystals, showed not only a greater degree of fall but also a definite prolongation of effect as compared with those following insulin of the amorphous type.

special test days, when they were carried out at hourly intervals from about 8 a. m. to 11 p. m. or midnight. Almost without exception, blood was obtained from puncture of an ear lobe.

Before actual studies were begun, the diabetic condition of the patients was stabilized on the diet to be followed during the investigation by appropriate doses of market samples of unmodified insulin-Lilly of the amorphous type. This preliminary period, during which no comparative studies were carried out, varied from five to sixteen days.

On the first day of the first test period food was withheld, and after samples of control blood and of urine had been secured a dose of the insulin to be tested was given subcutaneously (a carefully selected 0.5 cc. syringe with a scale-bearing portion 4 cm. long and graduated in 0.01 cc. divisions being used) and samples of capillary blood were taken thirty and sixty minutes later and then hourly for from fourteen to sixteen hours. The urine was collected at intervals of two hours and tested for sugar and acetoacetic acid. The quantity of sugar, and in five patients the quantity of nitrogen, was determined in each of the specimens. At the end of from fourteen to sixteen hours a midnight supper was given, preceded by a suitable dose of insulin. During the next few days, usually four, the patient was maintained on that type of insulin used on the initial test day. Then followed a second test period consisting of (*a*) an initial day on which food was withheld and a single dose of the second type of insulin under study was given and (*b*) days of maintenance, usually four, on the same type of insulin. Then the entire procedure was repeated for two more test periods, so that each type of insulin was used during at least two test periods with each patient. This elaboration of the familiar "cross-over" procedure used in animal work helps avoid

TABLE 1.—*Results of Assay of Insulin Preparations Used*

Type of Insulin	Manufacturer	p_H*	Units per Cc.†	Nitrogen, Mg. per 1,000 Units	Zinc,‡ Mg. per 1,000 Units,
Solution of zinc insulin crystals	Lilly,	2.82	40	0.0061	>0.2-<0.4
	Stearns	2.90	40	0.0073	0.3- 0.4
Insulin (prepared from amorphous material)	Lilly,	2.80	40	0.0077	<0.0125
	Stearns	2.74	40	0.0100	0.17-0.21

* The p_H determinations were carried out by Dr. O. H. Pearson in the department of biochemistry of the Harvard Medical School. They were made electrometrically with a glass electrode.

† Greatest possible difference from 40 is not more than about 5 per cent.

‡ The limits established for the zinc content of "insulin specially prepared as solution of zinc insulin crystals" are not less than 0.2 mg. and not more than 0.4 mg. per thousand units. The content of organic and inorganic impurities is likewise limited.

erroneous conclusions which may be drawn from improvement in carbohydrate tolerance due simply to long continued control of the diabetic condition. It aids also in minimizing the influence of the added care

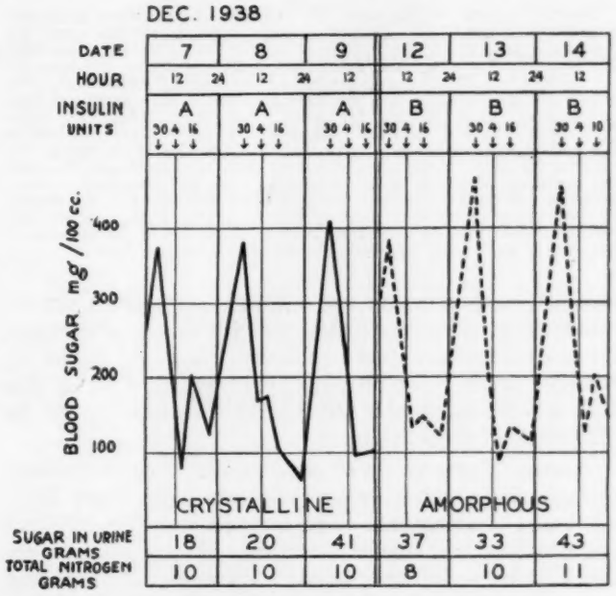

Chart 10 (case 5).—Response to insulin A (Lilly, solution of zinc insulin crystals) and insulin B (Lilly, amorphous type). Despite the more pronounced effect secured with the crystalline preparation in this patient, as shown in chart 9, the difference in effect on days of maintenance was slight. The blood sugar curves shown here were only slightly lower during the days of maintenance on insulin A (solution of zinc insulin crystals) than on insulin B (amorphous type), and the amount of sugar excreted in twenty-four hours was only slightly less when insulin A was used. The differences both as regards blood and urine sugar determinations are minimal. Again it is worth while to point out that insulin A (crystalline) given before the evening meal was inadequate to prevent fasting blood sugar values of 400 mg. per hundred cubic centimeters, or slightly less, fourteen hours later.

in treatment which both physician and patient often take when trying a new preparation.

The dosage of insulin given on the days of starvation was in four patients 0.15 unit per kilogram of

body weight. In case 2 0.165 unit and in three others (cases 1, 4 and 8) 0.2 unit per kilogram was given. During the days of maintenance insulin was given two, three or four times a day, as indicated by the condition of the patient. Every attempt was made to keep the dosage constant from day to day. Except for the special test days when patients were kept in bed, they

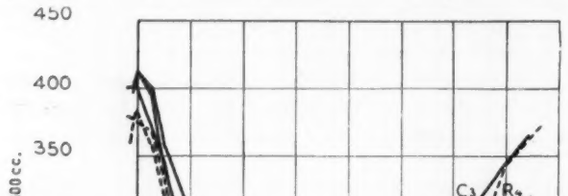

Chart 11 (case 6).—Blood sugar curves following single doses of insulin-Stearns (0.15 unit/Kg.). Food was withheld throughout the tests. C_1, crystalline, Jan. 31, 1939; R_2, amorphous, February 6; C_3, crystalline, February 11; R_4, amorphous, February 16; C_5, crystalline, February 21. Miss R. C., aged 20.8 years, had had diabetes since January 1927. The diet during the period of study was carbohydrate 168 Gm., protein 72 Gm., fat 65 Gm. Body weight, 139 pounds (63 Kg.); height, 64 inches (163 cm.). Curve C_1 was quite different from other curves obtained in this patient with the same type of insulin. The other four curves, two showing the effect of the solution of zinc insulin crystals and the other two the effect of insulin of the amorphous type, are remarkably similar, with the two curves following the amorphous preparation lying between the two following the crystalline preparation. One must conclude that, except for curve C_1, there was no essential difference in the response of this patient to the two types of insulin.

were allowed to be up and around. As far as practicable, the amount of physical activity was kept constant from day to day. Five patients (1, 2, 3, 4 and 5) received exclusively insulins made by Eli Lilly & Co. and the three others (6, 7 and 8) those made by Frederick Stearns & Co.

Normal Persons.—For studies on normal persons, eight healthy men (medical students aged from 21 to 24 years) were chosen. The tests on any given student were carried out one week apart. The subjects were asked to keep constant, as far as possible, the time and composition of the evening meal on the day preceding the test day. During the test day the amount of physical activity was minimal; for the most part the subjects lay quietly at rest. Smoking was prohibited. The body temperature was taken as a routine shortly after the beginning of the test. In only two instances was this slightly above normal (99.1 F. in each case), and in only one of these subjects was a cause evident (mild infection of the upper respiratory tract). Since the results of the tests on these days were not unusual, they were included in calculating the general average.

The "cross-over" procedure was employed: on the first test day a single dose of insulin of amorphous (or crystalline) type (0.15 unit per kilogram of body weight) was given subcutaneously and the response of the blood sugar noted by determinations of capillary samples at half-hourly intervals for the first three hours and then at hourly intervals for the next seven hours. The subjects reported for the tests after an over night fast of twelve hours, and food was withheld during the ten hours of the test day. On the second test day a week later, the other type of insulin was injected. On the third test day, the type of insulin used during the first day was again given and, on the fourth test day, the other type of insulin was administered. Therefore, with each subject four curves were obtained, two with insulin of the amorphous type and two with a solution of zinc insulin crystals. The type of insulin used on the first test day was varied from subject to subject. Four subjects received exclusively insulins made by Eli Lilly & Co. and four others those made by Frederick Stearns & Co.

Rabbits.—No extensive comparison of the insulins made from crystals and those made from amorphous material was carried out in rabbits because (*a*) Dr. Melville Sahyun [14] of Frederick Stearns & Co. had recently reported that average curves obtained when thirty-three rabbits for each type of insulin tested were almost identical and (*b*) comparisons in large groups of rabbits (from forty-eight to eighty-two animals in a given series of tests), made in the laboratories of the Insulin Committee of the University of Toronto on samples of the same lot numbers sent them by us, showed no significant difference in effect between the amorphous and the crystalline types of insulin. However, we thought it wise to secure some information at first hand and so compared the effect of the four types of insulin, i. e. the amorphous and the crystalline types from the two manufacturers—in each of ten rabbits, using the "cross-over" method. The tests were carried out after a fast of twenty-four hours. Only male rabbits of Dutch breed weighing from 1,500 to 2,140 Gm. were used. Insulin of U-40 strength in dosage of 0.8 unit per kilogram of body weight was injected

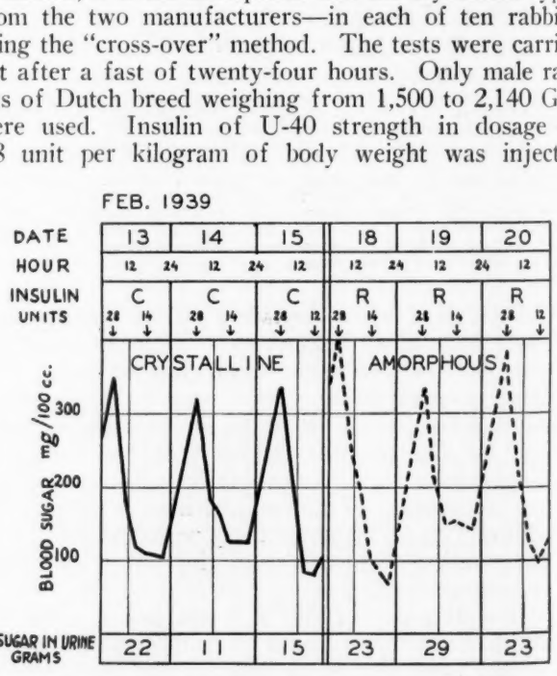

Chart 12 (case 6).—Response to insulin C (Stearns, solution of zinc insulin crystals) and insulin R (Stearns, amorphous type). The blood sugar curves during the three day periods of maintenance indicate a slightly greater effect of the crystalline preparation. This is borne out by the smaller amount of sugar in the urine.

subcutaneously, an "Agla" micrometer syringe being used. The capillary blood sugar was determined on samples from the marginal vein of the ear at half-hourly intervals for the first three hours and at hourly intervals for the next three hours. In the six days

between successive tests the animals were maintained on a diet of Park and Pollard rabbit pellets with weekly feedings of lettuce and carrots.

RESULTS

The results of the investigation are presented in the accompanying charts. In charts 1 to 16 [18] inclusive the results obtained with the eight diabetic patients are recorded in detail. The charts bearing odd numbers up to and including 15 show the blood sugar curves obtained with a single dose of insulin given subcutaneously on a day of rest and starvation. The values for sugar and nitrogen in the specimens of urine collected at intervals of two hours throughout these tests are not recorded because they add little of importance to the data on blood sugar. The charts bearing even numbers up to and including 16 show the daily blood sugar curves and the daily excretion of sugar and nitrogen in the urine during periods of maintenance on a given type of insulin. In the latter charts the portions that are reproduced are entirely unselected, representing in each instance the data obtained during the last two of the four or more study periods of each patient (except in case 3, in which complete data were not available). The results during the day following that of the special tests were uniformly excluded because the lower values for sugar in the blood and urine, which were then almost invariably obtained, were not consistent with those subsequently shown.

In all the charts, solid lines are used to indicate blood sugar values when solution of zinc insulin crystals was used, and interrupted lines those when insulin made from amorphous material was used. In chart 16 the dotted line shows the effect of protamine zinc insulin.

In chart 17 appear curves which represent composites of those obtained with the eight diabetic patients and shown in the odd numbered charts from 1 to 15 inclusive. The curve labeled "amorphous" represents the average of seventeen curves secured following a single injection of that type of insulin and the curve labeled "crystalline" represents the average of eighteen curves secured following a single injection of solution of zinc insulin crystals. It is obvious from chart 17 that both types of insulin must be considered as rapidly acting with a duration of effect much less than that recognized as characteristic of protamine zinc insulin. The effect of the solution of zinc insulin crystals, however, was definitely, although slightly, prolonged as compared with that of insulin made from amorphous material. In the curve showing the effect of the crystalline type, a slightly greater blood sugar lowering action was evident, and the lowest point occurred one hour later than in the other curve. In the return toward the initial value, a lag of approximately two hours occurred when the solution of zinc insulin crystals was used.

In chart 18 is shown the difference in the duration of effect between insulin of the amorphous type and that of solution of zinc insulin crystals in normal persons. The curves are essentially the same up to three hours after the administration of insulin; the rate of initial fall is the same except in the case of curve *B* (amorphous type of insulin). After the first three hours curves *C* and *A*, showing the effect of two brands of solution of zinc insulin crystals, exhibit a slower return toward normal than do the two curves showing the effect of the amorphous types. The latter pair of curves reaches a plateau at about six hours, whereas the former pair does so about eight hours after the giving of insulin. However, the differences in terms of actual blood sugar values are slight indeed.

From a study of chart 19, which presents the data secured with rabbits, no significant difference in duration of effect of either type of insulin, amorphous or crystalline, can be claimed. The curves are remarkably alike, considering the fact that the number of animals was small. With all four insulins the initial rate of fall was sharp and the lowest blood sugar level was reached

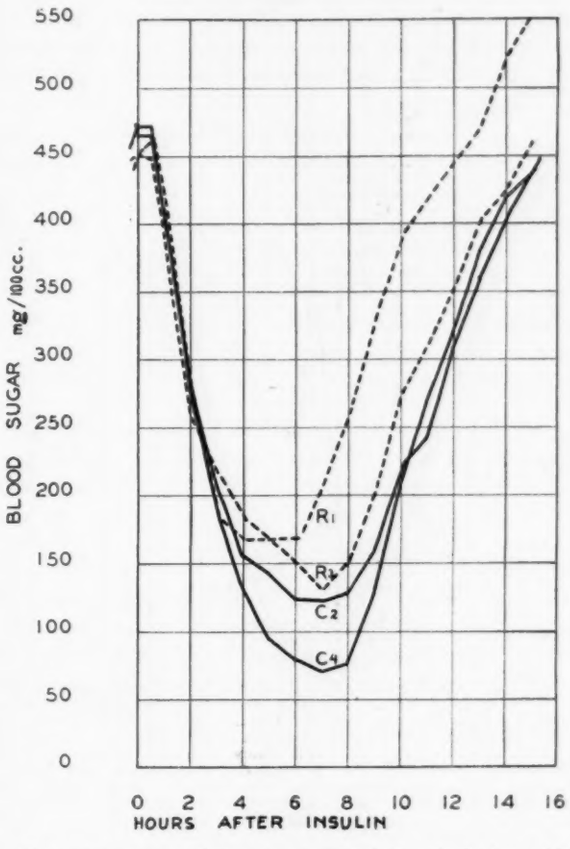

Chart 15 (case 8).—Blood sugar curves following single doses of insulin, Stearns (0.2 unit/Kg.). Food was withheld throughout the tests. R_1, amorphous, Feb. 11, 1939; C_2, crystalline, February 16; R_3, amorphous, February 21; C_4, crystalline, February 27.

Miss F. H. aged 28.7 years had had diabetes since December 1928. The diet during the period of study was carbohydrate 158 Gm., protein 80 Gm., fat 81 Gm. Body weight, 155 pounds (70.3 Kg.); height, 65½ inches (166 cm.). The rate of fall of the blood sugar was remarkably the same during each test, regardless of the type of insulin used. The solution of zinc insulin crystals exerted a somewhat greater hypoglycemic effect and a slight but definite prolongation of action.

in one and a half hours (with the possible exception in the case of curve *A*). The return of the blood sugar to normal took place at essentially the same rate in all cases, and at the end of five and six hours the points on the curves produced by the solution of zinc insulin crystals were slightly higher than those on the curves produced by insulin of the amorphous type of the same manufacturer.

COMMENT

It is apparent from the data just presented that the duration of effect of the solution of zinc insulin crystals is fully as great as, and on the whole somewhat greater than, that of insulin made from amorphous material. The prolongation of action is particularly evident in certain of the patients with diabetes. In an attempt to decide more definitely regarding the comparative duration of effect, we have analyzed the curves obtained

18. To save space, charts 3, 4, 5, 6, 7, 8, 13 and 14 have been omitted. They appear in the authors' reprints.

with the eight diabetic subjects on the special test days during which a single dose of insulin was given and food was withheld. As guides we have arbitrarily chosen two points on each curve: (*a*) That at which the blood sugar begins the return from the lowest value. This is usually the lowest point itself, except that we have regarded as insignificant a variation of 5 mg., thereby allowing for those instances in which the blood sugar remained at the lowest level for more than one reading. (*b*) That at which the blood sugar curve in its return to the initial value crosses the 180 mg. abscissa. The number of hours after the injection of insulin required for the curve to reach these points then serves to indicate the length of action of the preparation under study. We attempted also to determine the number of hours required for the complete return to the initial value, but since this occurred in only a few instances the average figures are not of significance. The average values for the two points just defined are given in table 2.

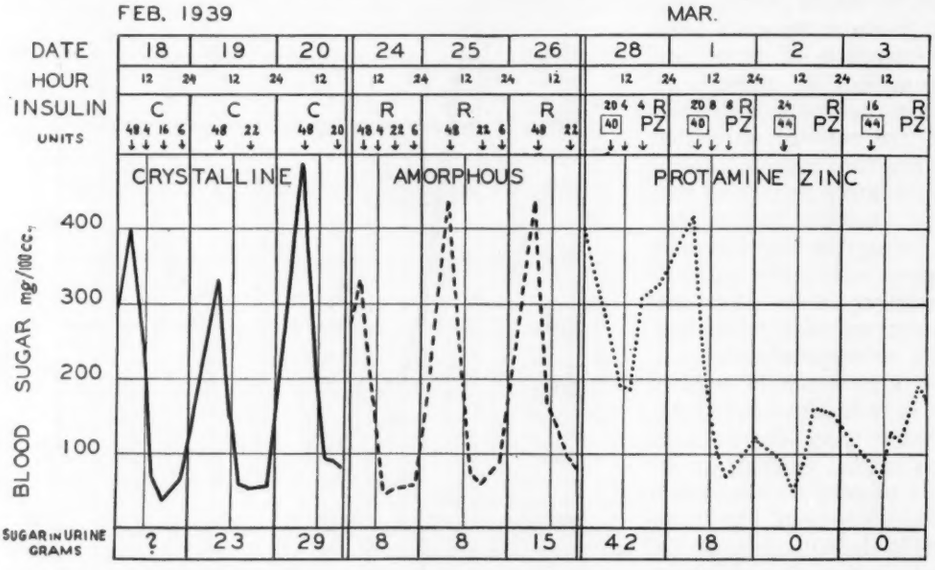

Chart 16 (case 8).—Response to insulin C (Stearns, solution of zinc insulin crystals) and insulin R (Stearns, amorphous type). The first two divisions of the chart show the blood sugar curves during three day periods of maintenance, first with the crystalline and then with the amorphous preparation. There was no essential difference; if one judges from the output of sugar in the urine, the degree of control was slightly better with insulin of the amorphous type. The third portion of the chart, in which the blood sugar curve is represented by a dotted line, is appended to illustrate what takes place when a type of insulin is used which truly has a prolonged action. On February 28 the patient was returned to our usual schedule of giving doses of unmodified insulin, amorphous type, plus a dose of protamine zinc insulin in the morning before breakfast (on this day and on March 1 small doses of unmodified insulin were given also before the noon meal and before the evening meal as indicated). In striking fashion the blood sugar values approached normal and the sugar disappeared from the urine. The total dosage of insulin on March 3 was 60 units, as compared with that of 74 units on February 18 when the solution of zinc insulin crystals was being used.

TABLE 2.—*Duration of Effect on Blood Sugar of Insulin Made from Amorphous Material and of Solution of Zinc Insulin Crystals Following a Single Injection*

	Time Required to Leave the Lowest Point		Time Required to Cross the 180-Mg. Abscissa	
	Number of Curves	Hours	Number of Curves	Hours
Amorphous	16*	7.0	11	9.6
Crystalline	18	7.8	13	11.2

* One curve (chart 13, curve R₂) was omitted because the value of four hours was obviously not representative.

It is evident that the action of the solution of zinc insulin crystals was slightly prolonged as compared with that of insulin of the amorphous type, but the difference was not great. As shown in table 2, the average value of seven hours as the time required to leave the lowest point was obtained with sixteen curves following the amorphous type in eight patients, whereas the corresponding average value in eighteen curves following the crystalline type in the same eight patients was 7.8 hours. Furthermore, it will be seen in table 2 that an average of 9.6 hours was required for the blood sugar on its return to the initial value to cross the 180 mg. abscissa; the corresponding value for the crystalline type was 11.2 hours.

From a clinical standpoint, of even more significance than the data just discussed are the results with the eight diabetic patients during the days of maintenance on the two types of insulin, as shown in the even-numbered charts from 2 to 16 inclusive. In the final analysis, the important consideration is whether, with given doses of one type of insulin, hyperglycemia and glycosuria are less than on the same doses of the other type. Casual inspection of these charts shows that there was very little difference between the degree of control secured with a solution of zinc insulin crystals and that with insulin made from amorphous material. Such slight differences as were apparent were usually on the side of slightly lower values for sugar in blood and urine while the solution of zinc insulin crystals was used. Closer study of these charts together with portions of them not reproduced in this paper leads to this same conclusion. The average number of grams of sugar excreted in the urine by eight patients during sixty-five days of maintenance on insulin of the amorphous type was 26 Gm., as compared with 18 Gm. by the same patients during sixty-seven days of maintenance on the same dosage of the crystalline type. It must be conceded that the difference between these two figures is slight, in view of the fact that the patients received from 137 to 247 Gm. of carbohydrate a day. Furthermore, the average daily excretion of nitrogen in the urine of five patients while maintained on the amorphous type was 14 Gm., the same as that during maintenance on the crystalline type.

It is worth while to point out again that in our studies of diabetic patients the rate of fall of the blood sugar in the four to six hours following a single dose of insulin was found to be essentially the same for the crystalline and the amorphous types. In other words, the rapidity of action seems essentially the same and, although we have no direct data on this point, there would appear to be no reason why a solution of zinc insulin crystals cannot be used when a quickly acting type is desired, such as in diabetic acidosis and coma. We agree with the suggestion that insulin of the crystalline type might well be made the quickly acting market insulin, supplanting the amorphous type. Theoretically at least it should give rise to fewer allergic

responses than the amorphous type, although at the present time certain market preparations of the latter type are of a high degree of purity. It seems to act slightly longer, and this is a further point of desirability, since no rapidity of action is sacrificed. It cannot, however, be regarded as an insulin with prolonged activity in the sense that protamine insulin, with or without zinc, is. It certainly does not act two or more times as long as the amorphous variety, and in the patient with severe diabetes a dose before the evening meal does not prevent hyperglycemia the following morning before breakfast. In our experience protamine zinc insulin remains the slowly acting, long lasting insulin of choice; in this respect solution of zinc insulin crystals cannot be compared with it.

SUMMARY

1. Detailed studies comparing the rapidity of action and duration of effect of unmodified insulin made from amorphous material and of solution of zinc insulin crystals were carried out on eight normal persons and on eight patients with severe grades of diabetes of long duration. Comparative tests were also made in a small series of rabbits.

2. Insulin from two manufacturers (Eli Lilly & Co. and Frederick Stearns & Co.) was used. The potency and zinc and nitrogen content of the samples of insulin were verified by determinations made in the laboratories of the Insulin Committee of Toronto.

3. Insulin made from amorphous material and insulin specially prepared as solution of zinc insulin crystals caused a prompt fall, almost identical in rate, of the blood sugar of both normal and diabetic subjects. Both must be regarded as rapidly acting insulins.

4. In normal rabbits the duration of action of insulin "specially prepared as solution of zinc insulin crystals" was almost identical with that of insulin made from amorphous material. In normal human subjects the action of the crystalline type appeared to be slightly prolonged. In diabetic patients a similar prolongation of effect was, in general, apparent. With the diabetic subjects there occurred on the average a slightly greater blood sugar lowering action following the crystalline type. The lowest point in the curve following a single injection was reached in six hours in the case of the amorphous and in seven hours in that of the crystalline variety. In the return to the initial value there was (up to fourteen hours after the injection) a lag of approximately two hours when the crystalline type was used.

Comparison of observations made during days of maintenance on the two types of insulin in similar dosage shows that the values for sugar in the blood and urine were on the average slightly less when a solution of zinc insulin crystals was used. The differences were of such slight degree as to be of minor significance clinically.

5. To simplify treatment for patients and physicians alike, it is advisable to decrease, rather than increase, the number of types of insulin on the market. At the present stage of development, it seems desirable to limit these to (*a*) a rapidly acting insulin which might well be prepared from crystalline rather than from amorphous material and (*b*) a slowly acting variety, the protamine zinc insulin.

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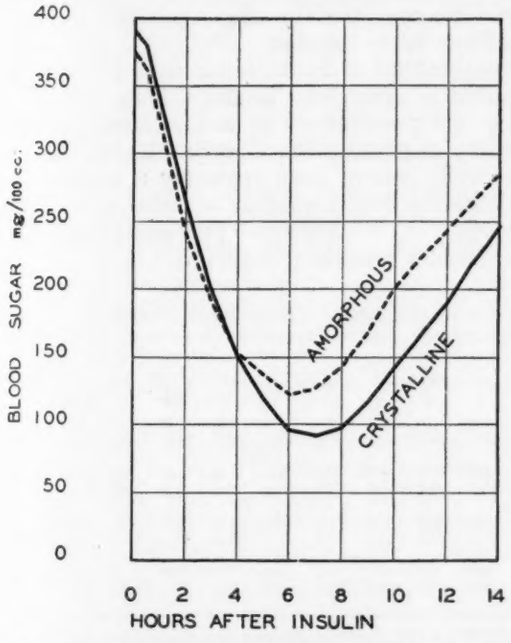

Chart 17.—Composite blood sugar curves showing the average response of eight diabetic patients to single subcutaneous doses of insulin of the amorphous type and of "insulin specially prepared as solution of zinc insulin crystals" (composites of curves in the odd numbered charts from 1 to 15 inclusive).

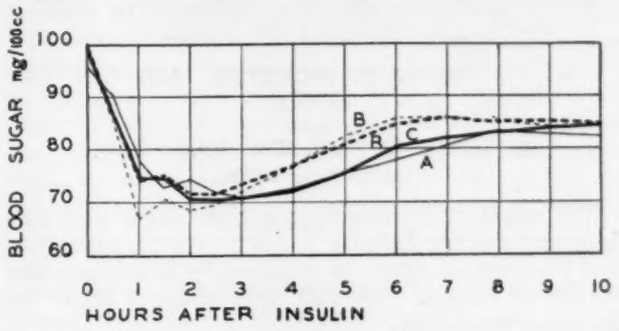

Chart 18.—The response of the blood sugar of normal persons to insulin following the subcutaneous injection of a single dose of 0.15 unit per kilogram of body weight. Food was withheld throughout the tests. Each curve represents the composite of eight curves, two for each of four persons. *A*, solution of zinc insulin crystals-Lilly; *B*, insulin-Lilly, amorphous type; *C*, solution of zinc insulin crystals-Stearns; *R*, insulin-Stearns, amorphous type.

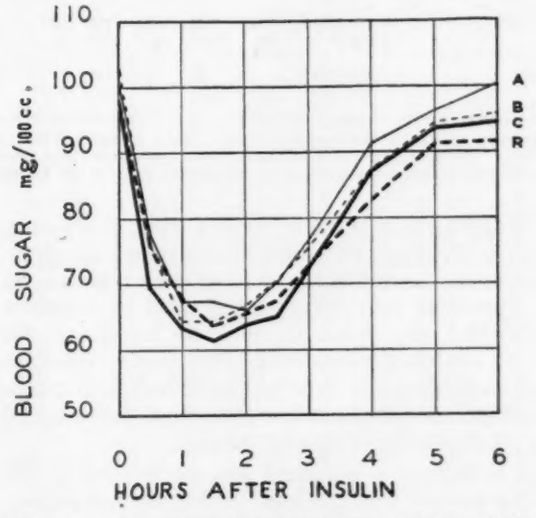

Chart 19.—The response of the blood sugar of fasting rabbits following a single dose of insulin injected subcutaneously in the amount of 0.8 unit per kilogram of body weight. Each curve represents average values obtained with ten animals. *A*, solution of zinc insulin crystals-Lilly; *B*, insulin-Lilly, amorphous type; *C*, solution of zinc insulin crystals-Stearns; *R*, insulin-Stearns, amorphous type.

SOLUTIONS OF AMORPHOUS INSULIN AND SOLUTIONS OF ZINC INSULIN CRYSTALS

CLINICAL STUDIES ON THE COMPARATIVE SPEED AND DURATION OF ACTION

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RUSSELL M. WILDER, PH.D., M.D.
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We submit the accompanying blood sugar time data from experiments designed to test the comparative speed and duration of action of solutions of amorphous and crystalline insulin. The data were obtained under the following conditions:

1. The subjects were eight patients with diabetes of different but previously established degrees of severity. The disease was of moderate severity in three cases and severe in five. In all cases it was of two or more years' duration and no patient had been under observation in the hospital for less than eight days immediately preceding any experiment. All but two patients had been under the supervision of one of us for one or more years.

2. For at least four days, and usually for from one to two weeks, before any experiment no insulin containing protamine was administered, a constant diet was fed and either two or three injections were given daily of one of the preparations of insulin under investigation. These injections were administered in such a way as to control glycosuria only incompletely and to insure a high value for the blood sugar each morning. No experiment was undertaken until a reasonably constant degree of postabsorptive hyperglycemia had been established, and an interval of not less than three days elapsed between all experiments on any subject.

3. The individual experiment was performed as follows: The patient was confined to bed on the experimental day and a single dose of the insulin to be tested was injected subcutaneously in a region of the skin not previously used for subcutaneous injections. The size of the dose was from one third to one half the previous morning dose of insulin. All subsequent tests of the same or of any other insulin on a given individual were made with the same dose. Uniformity of hydration of blood and tissues was sought by administering orally 500 cc. of water five hours before the injection of insulin and 150 cc. at hourly intervals beginning an hour before the injection and ending seventeen hours later. The insulin was injected at 8 a. m. and capillary blood was sampled for reducing power immediately before the injection [1] and at hourly or two hourly intervals thereafter until 8 p. m. or midnight; again in most cases at 2 or 3 a. m., and finally at 8 a. m., twenty-four hours after the injection. No food was given during the entire period.

4. At least two, and usually all, types of insulin employed were tested on each subject so that their effects could be compared in single patients as well as in all patients taken together.

5. The preparations of insulin tested were (*a*) a commercial solution of amorphous insulin ("iletin," insulin-Lilly); (*b*) two preparations of insulin from the Eli Lilly Company of composition unknown to us: insulin A and insulin B, one of them reputedly a solution of amorphous insulin and the other a solution of zinc insulin crystals; (*c*) a commercial preparation of solution of zinc insulin crystals (Stearns).[2]

TABLE 1.—*Average of Fall in Values for Blood Sugar After Injection of Different Preparations of Insulin*

		A. M.					P. M.										A. M.	
		8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	12	2 or 3	8
1. Amorphous insulin ("iletin," insulin-Lilly)*	Mg./100 cc.	0	41	107	159	194	216	213	213	193	185	153	157	119	124	111	89	44	+61
	Per cent	0	12.7	32.5	48.5	59.4	68.1	65.5	67.8	59.9	59.2	48.9	50.3	38.8	40.6	36.4	29.8	17.6	+1.0
2. Solution of zinc insulin crystals (Stearns)*	Mg./100 cc.	0	35	108	162	205	245	243	251	245	228	213	199	181	165	147	124	58	14
	Per cent	0	11.5	33.9	50.6	63.8	77.5	73.9	79.9	73.7	72.1	63.8	62.7	54.6	52.2	47.0	41.0	23.6	10.0
3. Insulin A†	Mg./100 cc.	0	48	112	172	205	222	235	227	225	200	183	165	150	139	129	112	88	27
	Per cent	0	14.0	34.4	53.6	64.6	72.7	73.2	73.8	69.2	64.6	56.4	53.7	46.8	45.6	42.8	38.0	30.6	12.1
4. Insulin B†	Mg./100 cc.	0	47	125	185	211	210	224	205	208	181	182	156	150	132	126	113	96	43
	Per cent	0	14.4	37.4	60.9	67.8	72.0	71.9	69.5	66.3	61.7	58.1	55.5	48.6	45.9	44.5	41.2	35.6	19.3

* Each figure represents the average of the results in from seven to four patients. Each patient served as the test object for both amorphous insulin ("iletin" insulin-Lilly) and solution of zinc insulin crystals (Stearns).

† Each figure represents the average of the results in from six to five patients. Each patient served as the test object for both insulin A and insulin B.

In table 1 is shown the average fall in values for blood sugar after injection of these preparations of insulin, the results being expressed both as milligrams per hundred cubic centimeters and as the percentage of the original level. These data are presented graphically in terms of percentage of decrease in blood sugar

From the Department of Medicine of the University of Chicago and the Mayo Clinic and Mayo Foundation.

Owing to lack of space, this article is abbreviated here by the publication of a condensed table instead of the complete tables, which appear in the authors' reprints.

Drs. Natalie Deyrup, Lester Odell and Russell M. Wilder Jr., of the University of Chicago Clinics, and Drs. Kendrick Smith and Samm H. Mann, of the Mayo Clinic, collected numerous samples of capillary blood. Dr. Wright Adams, of the Department of Medicine, and Mr. John Smith, of the School of Business, University of Chicago, gave valuable aid in the statistical analysis of our data.

This investigation was originally supported by a grant from the Eli Lilly Company for the sole purpose of studying the comparative speed and duration of action of their preparation known as "Iletin (insulin, Lilly)" and "Iletin (insulin, Lilly) specially prepared as Solution of Zinc-Insulin Crystals." As the study proceeded our interest prompted us to subject other preparations of insulin to the same tests. No support was received for any part of the work done in Rochester.

1. The analytic methods for determining the reducing power of the blood were the method of Miller and Van Slyke (J. Biol. Chem. **114**: 583, 1936) in the experiments performed at the University of Chicago and the Folin ferricyanide method (J. Biol. Chem. **77**: 421, 1928) in the experiments at Rochester.

2. The package containing insulins A and B was sent to one of us (H. T. R.) by the Eli Lilly Company. It was opened in the presence of Dr. Paul Leech, secretary of the Council on Pharmacy and Chemistry of the American Medical Association. Samples of both insulins were removed by Dr. Leech for analysis (see footnote 4), and of the remaining bottles some were taken to the University of Chicago for clinical trial and some were sent to Rochester for the same purpose. Samples were also sent to Dr. T. G. Klumpp, of the Food and Drug Administration, Department of Agriculture, Washington, D. C. The commercial solution of amorphous (regular) insulin ("iletin," insulin-Lilly) was purchased in the open market and bore the lot number K8-971246-X2. The solution of zinc insulin crystals (Stearns), also purchased in the open market, bore the lot number C-2702-K. All preparations tested were approximately of U-40 concentration. Mr. F. Lorne Hutchison, secretary of the Insulin Committee of the University of Toronto, reported in a personal communication that on the basis of assays on bulk batches this preparation of "iletin" (insulin-Lilly), contained about 41 units per cubic centimeter and the Stearns product about 40¾ units per cubic centimeter. Further assays made by the Insulin Committee on the actual lot numbers used by us were reported as showing the two insulins to be "very similar in potency."

in chart 1, in which the effect of amorphous insulin ("iletin," insulin-Lilly) is compared with that of solution of zinc insulin crystals (Stearns), and in chart 2, in which is compared the effect of insulin A with that of insulin B.

It is apparent from lines 1 and 2 in table 1 and from chart 1 that there are appreciable differences after 12 o'clock noon between the average percentage of fall

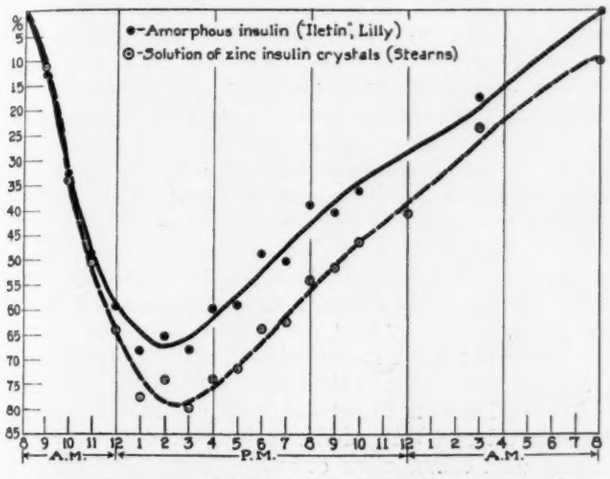

Chart 1.—Percentage of fall in values for blood sugar after injection of solution of amorphous insulin ("iletin," insulin-Lilly) and solution of zinc insulin crystals (Stearns). Each point represents the average of the results in from seven to four patients (lines 1 and 2 in the table). The two insulins were tested on each subject. The points about the curves show an unduly wide scatter because of the fact that from 12 noon to 8 p. m. specimens for blood sugar were taken only every second hour in the three Rochester patients whereas they were taken every hour in the four University of Chicago patients. Specifically, there are no data for the Rochester group for the hours 1, 3, 5, 7, 9 and 10 p. m. and midnight. The individual blood sugar curves were much smoother than these average curves would indicate.

in values for blood sugar after injection of solution of zinc insulin crystals (Stearns) and the average percentage of fall in such values after injection of amorphous insulin ("iletin," insulin-Lilly). These differences, however, are not sufficiently large to render it certain that they are real or important. The mean difference for each hour, therefore, was calculated from the original data and the resulting data were analyzed by statistical methods.[3] The analysis shows that for the hours 1, 2, 3 and 4 p. m. the differences observed possess statistical significance ($P < 0.05$). The average of the mean differences for each individual also proved to be significant.

There was, on the other hand, no significant difference between the values for insulin A and those for insulin B (lines 3 and 4 in table 1 and chart 2).

Our interpretation of the results of these experiments is influenced by the following considerations:

Although our procedure was designed to insure uniformity of experimental conditions, it must be recognized that the physiologic status of any diabetic patient probably varies from one day to another. Thus, although we aimed at having the postabsorptive value for the blood sugar at the beginning of each experiment on any one subject the same, we were not always successful in accomplishing this. It is for this reason that it has been necessary to express our results in terms of decrease in values for blood sugar from the fasting level in each experiment rather than in terms of absolute values for blood sugar. Again, it is evident from the data of individual patients that when the same insulin was tested twice on the same subject the results, while comparable, were never identical. This fact renders it probable that any differences which might be observed under the conditions of our experiments would need to be relatively large to be important clinically. Finally, we realized early in the course of this study that repeated days of starvation, even though separated by periods of several days during which the subject's usual diet was fed, might lead to progressive improvement in the patient's diabetes so that his response to insulin might differ in the first experiment as compared with the last. Some evidence of such an effect was observed in a few of the milder cases but it was not apparent in most. In an effort to avoid this difficulty, the order in which the various insulin preparations were tested was changed from patient to patient.

In spite of these difficulties, the experimental procedure we have employed involves fewer variables than tests of insulin action made when patients are receiving food or when they are ambulatory and physical activity is not controlled. We believe, therefore, that our results justify the following comments:

The most conspicuous feature of the blood sugar time curves which may be constructed from our data is the relative constancy of the rate of decline of the values for blood sugar during the first three hours of each experiment. This we interpret as indicating that the speed of activity of solutions of zinc insulin crystals is as great as that of solutions of amorphous insulin.

In certain individual experiments the blood sugar remained at a low level longer after injection of a solution of zinc insulin crystals (Stearns) than after injection of preparations of amorphous insulins, although this result was obtained inconstantly. Also the averaged data of the experiments in which this product was used would appear to show a slight but statistically significant increase in duration of effect. The prolonga-

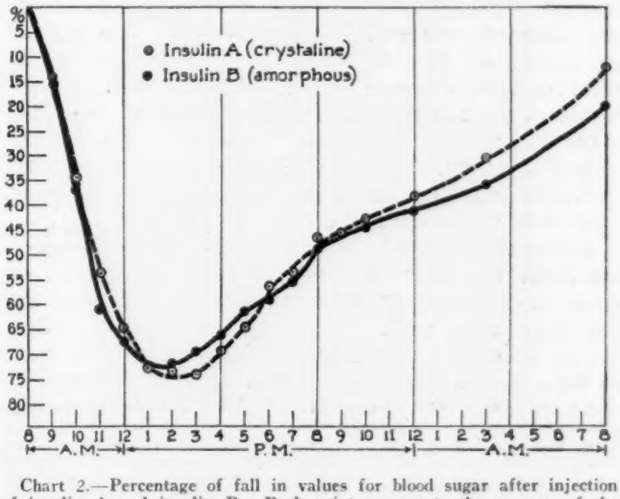

Chart 2.—Percentage of fall in values for blood sugar after injection of insulin A and insulin B. Each point represents the average of the results in from six to five patients (lines 3 and 4 in the table). The two insulins were tested on each subject.

tion of action, however, is not marked and its importance in the ordinary treatment of diabetes mellitus is yet to be ascertained.

Our figures give no indication of any definite difference of speed or duration of action between the two "unknown" products sent to us by the Eli Lilly Company. After the experiments were completed we were

3. Fisher, R. A.: Statistical Methods for Research Workers, Edinburgh, Oliver & Boyd, 1934.

informed by the Eli Lilly Company that insulin A was a solution of zinc insulin crystals and "insulin B" was a solution of amorphous (regular) insulin.[4]

CONCLUSIONS

Blood sugar time data obtained after the injection of single doses of insulin given without food to diabetic patients in the postabsorptive state failed to disclose material differences in speed or duration of action between solutions of amorphous (regular) insulin and solutions of zinc insulin crystals supplied by the Eli Lilly Company. The average of all data obtained by the injection of solution of zinc insulin crystals (Stearns) shows a slight but statistically significant prolongation of action, though no difference in speed of action, when compared with the average of all data obtained after injection of amorphous insulin. This difference was not apparent in all patients, and it does not seem likely that a prolonged effect of such small degree, obtained inconsistently, can represent a difference of clinical importance.

LANDMARKS IN SIMPLE PLEURAL EFFUSIONS

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Modern methods of examination have greatly facilitated the diagnosis of pleural effusion, particularly radiography. In spite of this it is nothing unusual for experienced clinicians to be embarrassed by a "dry tap" when there is clearcut evidence of pleural effusion. Nor is the embarrassment lessened when a successful thoracentesis is performed on the patient on the same day by another clinician who elected to introduce his needle one or two interspaces higher.

In most instances "dry taps" in simple effusions are due to the eagerness of the operator to remove every ounce. The patient is placed in the sitting position regardless of his physical condition, and the needle is introduced at a low level, frequently so low that it encounters diaphragm instead of liquid. One of the chief reasons for failure in thoracentesis is that the landmarks of the effusion are not clearly established. This is particularly true of the more common type, the simple pleural effusion, which is to be distinguished from hydropneumothorax and from cases in which tumor and adhesions complicate and distort the picture.

Before the advent of the x-rays many clinicians described the upper level of effusions as curved or straight, depending entirely on the upper margin of the flat percussion note. Probably one of the earliest descriptions is the curved line of Damoiseau [1] mentioned in most of the foreign textbooks. In this country we are taught the curved line of Ellis.[2] As shall be shown, neither of these lines truly represents the upper level of the effusion.

The ordinary roentgenographic appearance of simple pleural effusions is exemplified in figure 1 *A*. Here is seen a dense shadow at the base of the right lung field. The top of this shadow curves upward and outward from the hilus to the sixth rib in the axilla. By introducing air into the pleural space the simple effusion or hydrothorax becomes converted into hydropneumothorax (fig. 1 *B*). It is noted that the upper level is now a straight horizontal line. The explanation for this phenomenon has been considered in a previous article.[3] The horizontal line noted in hydropneumothorax describes accurately the upper level of the effusion. On percussion from above downward there is an abrupt change from hyperresonance to flatness. In simple effusions, however, both radiographic and physical signs are not quite so distinct. The percussion note changes from normal to dulness and flatness. It is extremely difficult accurately to locate the upper level of the effusion; this difficulty also applies to the roentgenogram.

It was not until a radiopaque oil was employed that it was possible to locate the upper level of the effusion. This experiment is illustrated in figure 2. Following the removal of 10 cc. of the pleural effusion an equal volume of a combination of iodized poppyseed oil and cajuput oil was replaced. The oil immediately floated to the top, as seen in figure 2 *B*, its highest point being on the same level with the outer tip of the curved dense shadow and definitely above the hazy shadow. The same result was obtained also in the anterior and posterior oblique views. It would appear from these observations as well as from our clinical knowledge that in simple pleural effusions the lung is surrounded by liquid.

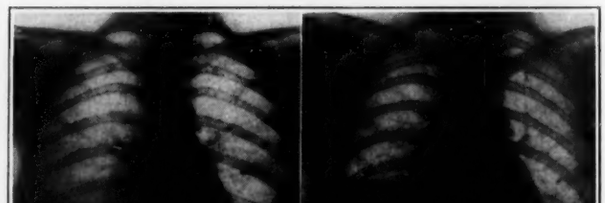

Fig. 1.—*A*, characteristic simple pleural effusion. Note the dense radiographic shadow curving concavely upward from the hilus to the axilla and the hazy shadow immediately above. *B*, same case after injection of air into the pleural space. Note the straight horizontal line and the absence of the hazy shadow.

The effusion may be compared with an irregularly shaped bowl in the hollow of which is the lung and surrounding which are the chest wall, mediastinal structures and diaphragm. The radiographic shadow cast by the bowl appears very dense at the bottom and sides and least dense in the hollow where aerated lung is interposed.

For the sake of convenience I have divided simple pleural effusions into three radiographic zones,[4] as follows, described from below upward:

1. A radiopaque zone, the area below the lung, visualized as a dense shadow.

4. This information was confirmed by Dr. E. W. Schoeffel of the chemical laboratory of the American Medical Association, who reported as follows: "Insulin A in solution displays the reaction generally exhibited by Eli Lilly's new crystalline zinc insulin in solution. Insulin B in solution behaves similarly to ordinary insulin in solution but does differ in several respects from the commercially available product. In conclusion, it can be said that insulin A approaches crystalline zinc insulin in solution. Insulin B approaches ordinary insulin plus a small surplus of unidentified matter." The batch represented by insulin A and the batch represented by insulin B were supplied for our clinical experiments because of the fact that, according to assays of samples of these two batches by the manufacturer and in the laboratories of the Insulin Committee of the University of Toronto, insulin A and "insulin B" would be of essentially identical strength, any slight difference of this from a strength of 40 units per cubic centimeter being approximately the same for the two insulins.

From the Medical Service, Sea View Hospital.

1. Damoiseau, H.: Recherches cliniques sur plusieurs points du diagnostic des epanchements, Extrait des Archives générales de médecine, 1844; from Garland, G. M.: Pneumo Dynamics, p. 2.

2. Ellis, Calvin: Boston M. & S. J. **90**: 13, 1874.

3. Kaunitz, Julius: Liquid Levels and Other Liquid Surfaces in Pleural Effusions, J. Thoracic Surg. **4**: 300 (Feb.) 1935.

4. Kaunitz, Julius: The Three Zones of Simple Pleural Effusions, Am. J. Roentgenol. **35**: 57 (Jan.) 1936; The Three Radiographic Zones of Simple Pleural Effusions, Brit. J. Radiol. **9**: 644 (Oct.) 1936.

2. A radiotranslucent zone, the area between the lung and chest wall, seen as a hazy shadow but dense in the lateral aspect.

3. A radiotransparent zone, the area of liquid between the lung and chest wall too thin to cast a shadow except in its lateral aspect.

The volume of liquid at the various levels of the second and third zones is easily gaged by observing the curved dense shadow as it tapers off from below upward.

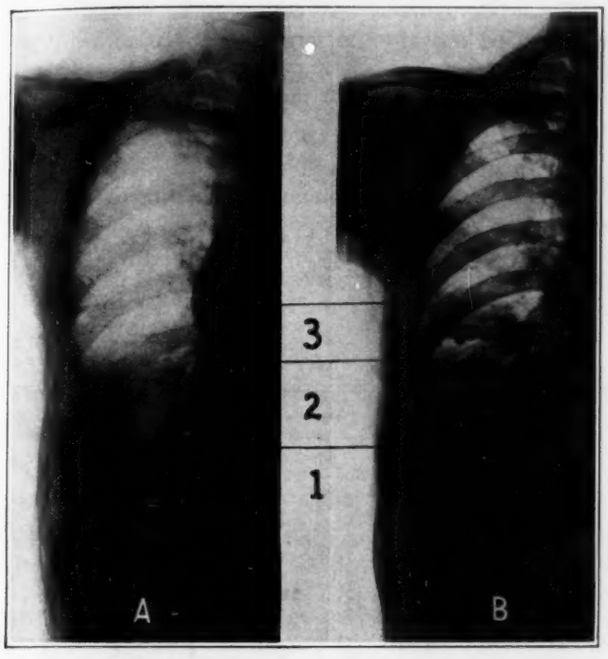

Fig. 2.—*A*, simple pleural effusion, as in figure 1 *A*. *B*, same case immediately after 10 cc. of effusion was replaced by an equal volume of radiopaque oil. Note the ascension of the oil into the clear field above the hazy shadow. The effusion is divided into three radiographic zones (for explanation see text).

This curved shadow is in fact a side view of that portion of the effusion interposed between the lung and chest wall, the tip of the curved shadow representing the upper margin of the effusion.

With the three zones as a landmark it is possible with a greater degree of accuracy to choose the site for thoracentesis. In effusions of moderate size it has been my custom to insert the aspirating needle at a point corresponding to the junction of zones 1 and 2 in the posterior axillary line. This corresponds to the beginning of absolute flatness in percussion. Aspirating below this point may be successful with large effusions; in small effusions the diaphragm may be encountered and may not be recognized, particularly on the right side where the flat percussion note over the liver merges with that over the effusion and the dense homogeneous x-ray shadow includes diaphragm, liver and effusion.

When feebleness of the patient precludes aspiration in the erect position, the reclining position may advantageously be employed. The usual procedure in right-sided effusions is to place the patient on his right side at the edge of the right side of the bed, and vice versa in left-sided effusions. The needle is inserted in an interspace near the posterior axillary line. In this position the liquid will gravitate downward from between the lung, mediastinum and diaphragm and permit almost complete aspiration.

Although the liquid is not as freely movable in simple pleural effusion as in hydropneumothorax, it does however change its position with the chest. These changes have been thoroughly described by Rigler.[5]

It is of interest to note that small effusions may entirely be hidden in the ordinary postero-anterior roentgenogram. In figure 3 *A*, taken in the erect position, a slight clouding in the right costophrenic sinus is seen. This small shadow suggests that a minute amount of effusion is present, "a teaspoonful" as many would describe it. When I injected 300 cc. of saline solution in a chest of normal adult size I was not able to obtain any shadow in the costophrenic sinus. Emerson and Ganter, as mentioned by Rigler, were unable to obtain radiographic evidence of effusion in the presence of 250 cc. and 450 cc. respectively. The liquid is probably concealed by the liver and diaphragm in the posterior costophrenic sinus. A shadow in the lateral costophrenic sinus is therefore indicative of the presence of at least 250 cc. of effusion in a normal sized chest. By changing the position of the patient it is possible to visualize some of the liquid concealed by the liver and diaphragm. Figure 3 *B* (same case as figure 3 *A*) was taken in the right decubitus position, and here a considerably greater amount of effusion may be visualized appearing as a ribbon-like shadow along the right border of the lung. This small effusion might easily be aspirated in this position for diagnostic purposes.

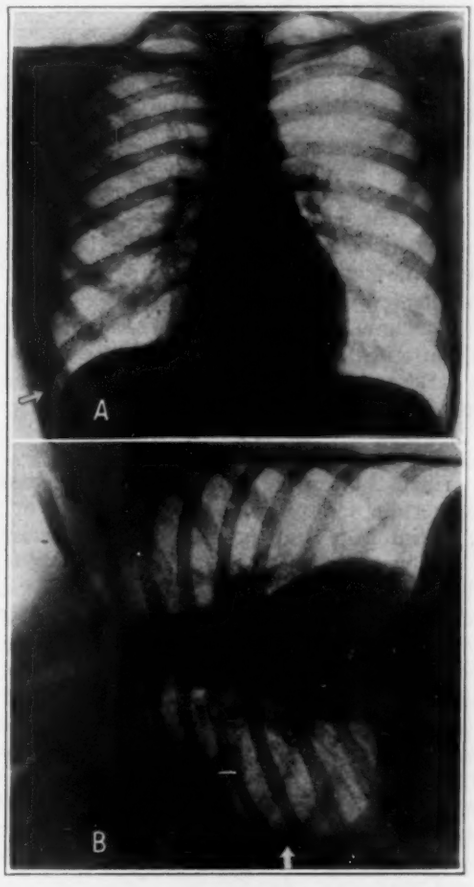

Fig. 3.—*A*, erect position, a small pleural effusion is suspected because of the slight clouding in the right costophrenic sinus. *B*, same case; right decubitus position; note the ribbon-like shadow extending along the lateral lower border of the right lung.

CONCLUSIONS

It is important to know the landmarks of a pleural effusion before attempting thoracentesis.

5. Rigler, Leo G.: Roentgen Diagnosis of Small Pleural Effusions: A New Roentgenographic Position, J. A. M. A. **96**: 104 (Jan. 10) 1931.

By special roentgenographic technic it was established that the simple pleural effusion extends well above the area of percussion flatness and above the dense radiographic shadow.

On the basis of distinct radiographic zones in simple pleural effusions, several principles have been formulated for locating with greater accuracy the site for thoracentesis.

1 West Eighty-Sixth Street.

THE TREATMENT OF PNEUMOCOCCIC PNEUMONIA WITH CONCENTRATED RABBIT SERUM

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AND
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There have been few reports submitted concerning the use of rabbit serum in the type specific therapy of pneumonia. This is particularly true of the concentrated and refined serum. The steadily increasing improvements in the character of the serum have indicated the fulfilment of the factors defining a good serum for therapy; namely, first that the intravenous administration be without undue reaction and second that the adequate dose be contained in a small volume. The theoretical and practical advantages that antipneumococcus rabbit serum possesses over horse serum have been pointed out by several observers.[1] These observations, however, have been made with the unconcentrated rabbit serum. Finland and Brown [2] describe the use of the concentrated serum in sixteen cases with two deaths in type I pneumonia. The present report deals with the administration of concentrated and refined rabbit serum in 153 patients, comprising twenty-one different types of pneumococcic infection.

CASE SELECTION FOR SERUM

The principal criterion for the selection of cases suitable for serum therapy was the availability of serum. Owing to the large number of pneumonia patients, the serum supply was generally inadequate. Consequently control comparisons were easy to obtain, practically of an alternate case character. These control data are found in table 2. Serum was not refused even when the outlook was very bad, such as the presence of pulmonary edema or duration of the disease of five or six days, factors which elevate death rate percentages. A positive Francis test or an otherwise good prognosis was frequently utilized to conserve our serum supply for the more necessary or urgent indications. Unquestionably the mortality percentage is thus higher in our series than it would be if a more rigid selection had been employed.

From the Cook County Hospital and the Department of Medicine, Loyola University School of Medicine.

The Pneumonia Committee of the Cook County Hospital and the attending physicians and resident staff cooperated with the authors in this work. The serum used was supplied by the Lederle Laboratories, Inc., the Illinois State Department of Public Health and E. R. Squibb & Sons.

1. Goodner, Kenneth; Horsfall, F. L., and Dubos, R. J.: Type Specific Antipneumococcic Rabbit Serum for Therapeutic Purposes, J. Immunology **33:** 279 (Oct.) 1937. Horsfall, F. L.; Goodner, Kenneth; MacLeod, C. M., and Harris, A. H.: Antipneumococcus Rabbit Serum as a Therapeutic Agent in Lobar Pneumonia, J. A. M. A. **108:** 1483 (May 1) 1937. Horsfall, F. L.; Goodner, Kenneth, and MacLeod, C. M.: Antipneumococcic Serum as a Therapeutic Agent in Lobar Pneumonia, New York J. Med. **38:** 245 (Feb. 15) 1938. Loughlin, E. H.; Bennett, R. H., and Spitz, S. H.: Treatment of Lobar Pneumonia with Rabbit Antipneumococcus Serum, J. A. M. A. **111:** 497 (Aug. 6) 1938. Bullowa, J. G. M.: Management of Pneumonias, New York, Oxford University Press, 1937.

2. Finland, Maxwell, and Brown, J. W.: Specific Treatment of Pneumococcus Type I Pneumonia, Am. J. M. Sc. **197:** 151 (Feb.) 1939.

METHODS OF STUDY

Typing was accomplished by the Neufeld method, applied directly to the sputum. Blood cultures were taken as a routine. Lung puncture, sputum culture and mouse inoculation were employed when difficulties with direct sputum identification were encountered. Repetition of the bacteriologic investigation was performed when the improvement expected did not result, in order to detect possible mistakes in the initial typing.

The intracutaneous test with specific polysaccharide was carried out after serum had been used whenever possible in those cases in which a negative Francis reaction had been present before serum was given.

SENSITIVITY TESTS AND UNTOWARD REACTIONS

The history of possible sensitivity was thoroughly investigated. The ophthalmic test for sensitization was employed as a routine. A positive test was not encountered in the entire series. The intracutaneous testing for rabbit serum sensitivity was discarded early in the investigation because of the frequency of positive readings, especially since we found that the administration of serum in these cases did not result in immediate reactions. No positive intravenous pressor reactions occurred. Difficulty was encountered especially in evaluating pulse rate changes during the course of the pressor test. The significance of this procedure is considered doubtful. We have not encountered an immediate reaction in the entire series.

TABLE 1.—*Types of Serum Treated Cases*

Type of Pneumonia	No. of Cases	Deaths		Bacteremia		
		No.	Per Cent	No.	Dead	Per Cent
I	30	2	6	6	1	16.7
II	34	3	8.8	6	3	50
III	14	3	21	0	0	0
IV	11	1	9	2	0	0
V	2	0	0	1	0	0
VI	1	0	0	0	0	0
VII	26	2	7.6	3	1	33
VIII	16	3	18	0	0	0
XII	2	0	0	0	0	0
XIV	2	1	50	1	1	100
XV	1	0	0	0	0	0
XVII	1	0	0	0	0	0
XVIII	3	0	0	1	0	0
XIX	1	0	0	0	0	0
XX	1	0	0	0	0	0
XXIII	1	0	0	1	0	0
XXIV	1	0	0	1	0	0
XXV	2	0	0	0	0	0
XXVIII	1	0	0	0	0	0
XXIX	2	0	0	1	0	0
XXXI	1	0	0	0	0	0
Totals	153	15	9.8	23	6	26

Corrected mortality (4 deaths under 18 hours) 11 deaths, 7.2 per cent

Thermal reactions were studied carefully because of their great frequency in the early phases of this study. This corroborates the observations of other investigators using rabbit serum. While the inherent thermogenic properties of the serum are very important, the controllable factors in this type of reaction are numerous. The rapid administration or dilution of the serum was found to be the important feature in producing chill and elevation of temperature. There was very little constancy or relationship to the particular injection in the divided dose method. This led us to try the single total undiluted dose method. The advantages of this procedure are obvious. The concentrated refined rabbit serum lends itself admirably to this technic, especially in the highly

concentrated unitage. It soon became apparent that the serum could be given at a more rapid rate without danger. The procedure now is to administer the first cubic centimeter in a period of two minutes, then the entire remainder at a rate of 1 cc. a minute. If the

TABLE 2.—*Control Types of Cases Not Treated with Serum*

Type of Pneumonia	No. of Cases	Deaths		Bacteremia		
		No.	Per Cent	No.	Dead	Per Cent
I	49	13	26	10	4	40
II	34	16	47	6	4	67
III	18	11	61	1	1	100
IV	3	2	67	0	0	0
V	6	5	83	4	3	75
VI	2	0	0	0	0	0
VII	17	6	35	4	4	100
VIII	8	1	12	2	1	50
IX	3	1	33	0	0	0
X	1	0	0	0	0	0
XII	5	2	40	1	0	0
XIII	2	0	0	1	0	0
XIV	2	0	0	0	0	0
XVI	1	0	0	0	0	0
XVII	2	0	0	0	0	0
XVIII	2	2	100	0	0	0
XIX	5	2	40	1	1	100
XXI	1	0	0	0	0	0
XXIII	1	1	100	0	0	0
XXVIII	1	1	100	0	0	0
XXIX	1	0	0	0	0	0
Totals	164	63	38.4	30	18	60

patient is receiving intravenous fluid at the moment serum administration is decided on, the needle of the syringe containing the total dose is pushed through the latex tubing near the intravenous needle and the serum is given at the rate already indicated. Otherwise the serum is given intravenously, directly from the syringe

TABLE 3.—*Age Distribution of Serum Treated Patients*

Age Group, Years	Number of Patients	Deaths
1-10	2	0
11-20	12	1
21-30	20	1
31-40	47	3
41-50	39	7
51-60	26	2
61-70	3	0
71-80	3	0
81-90	1	1
Over 50	33	3

TABLE 4.—*Race and Sex Distribution of Serum Treated Patients*

Race and Sex	Number	Deaths
A. White		
Male	75	7
Female	17	0
B. Negro		
Male	41	5
Female	14	1
C. Mexican		
Male	5	2
Female	0	0
D. American Indian		
Male	1	0
Female	0	0
Total		
Male	122	14
Female	31	1

at the indicated rate. One is cautioned to aspirate a minimal amount of blood into the syringe to indicate the intravenous position of the needle. The last sixty-nine consecutive patients in this series were treated by the single total undiluted dose technic with an incidence of only 8 per cent of thermic reactions compared to 28 per cent in our preceding eighty-four cases. With the highly concentrated unitage, this method requires only from ten to twenty minutes. A maximum of 35 cc. as the initial and total dose was given in this way without thermic reaction. A unitage concentration of 5,000 per cubic centimeter or over is particularly adaptable. We have tested the practicability of this method by having twelve interns inject sixty-nine patients. We believe that the therapeutic efficiency of the serum is enhanced by this method of administration.

Serum sickness (delayed reactions), such as arthralgia, urticaria and fever, occurred in 28 per cent of the cases. There was no relationship between the thermic reactions and the frequency of serum sickness.

CLINICAL RESULTS

This statistical study from the Cook County Hospital of a series of 153 patients with pneumococcic pneumonia treated by type specific antibody rabbit serum demonstrates a death rate less than one third, almost one fourth, that of the non-serum treated mortality. The

TABLE 5.—*Lobe Distribution of Serum Treated Patients*

Lobe	Number	Deaths
Right upper	17	3
Right middle	10	1
Right lower	53	4
Left upper	8	1
Left lower	42	3
Multilobar	23	3

TABLE 6.—*Relationship of Duration of Disease to Mortality of Serum Treated Patients*

Day of Disease Serum Was Given	Number	Deaths	
		Number	Per Cent
1st	6	0	0
2d	29	3	10.3
3d	44	1	2.2
4th	39	6	15.3
5th	23	3	13.0
6th	6	0	0
7th	3	1	33.0
8th	3	1	33.0

figures in tables 1 and 2 illustrate this rather vividly. Of the fifteen deaths that resulted, four occurred within eighteen hours after the administration of serum. If these deaths are removed from the statistics the death rate would be lowered to 7 per cent. The control series approximates very closely the serum treated figures in the several important variables, namely age, type of pneumococcic infection, bacteremia and seasonal incidence. There were thirty positive blood cultures in the control cases and twenty-three in the serum treated cases.

Table 3 shows thirty-three serum treated patients over 50 years of age with three deaths. These include eight type III cases with two deaths and nine type II pneumonias with one death.

A study of the temperature curves following serum administration in the patients who recovered shows a descent to normal within eighteen hours, a crisis termination, in seventy-seven patients. Normal temperature readings appeared in a forty-eight hour period in sixty-one cases.

An analysis of the deaths reveals the following important data: Fifteen deaths occurred. Four of these were

of bacteremic patients. Four occurred within eighteen hours after admission. No autopsies were permitted on these four. Autopsy showed in two patients suppurative pericarditis and in the remaining patient an acute pneumococcic endocarditis type VII. Deaths were restricted to types I, II, III, IV, VII, VIII, XIV (table 1).

COMPLICATIONS

This series shows relatively few complications. This tends to confirm the observations that there is probably an advantage in the penetrating and diffusing properties due to the smaller size of the rabbit serum pneumococcus antibody. Empyema occurred in five patients, all of whom recovered. Two patients with pericarditis and one with acute endocarditis died. One patient with acute suppurative otitis media complicated by meningitis with type IV pneumococcus obtained from the spinal fluid recovered. There were two other cases of otitis media, one showing extension to the mastoid. The usual supportive and symptomatic measures were utilized in the general treatment. Digitalis was not employed.

Intravenous fluids and oxygen were liberally administered. The need for these measures was distinctly less-

TABLE 7.—*Dosage Analysis (Includes Total and Repeated Doses)*

	Dosage					
	Cc. per Patient			Units per Patient		
Type of Pneumonia	Average	Maximum	Minimum	Average	Maximum	Minimum
I	33.5	120	10	123,800	250,000	100,000
II	27	55	14	117,600	240,000	46,500
III	51.8	120	12	135,000	180,000	100,000
IV	26	40	15	155,600	231,000	92,500
V	20	20	20	120,000	120,000	120,000
VI	20	..	..	160,000		
VII	21.6	50	5	210,000	450,000	70,000
VIII	27.6	40	18	139,300	180,000	70,000
XII	38.5	40	37	116,000	120,000	111,000
XIV	38	40	36	180,000	180,000	180,000
XV	100	..	..	400,000		
XVII	20	..	..	60,000		
XVIII	33	40	20	133,000	160,000	80,000
XIX	41	..	..	165,000		
XX	40	..	..	200,000		
XXIII	40	..	..	120,000		
XXIV	80	..	..	240,000		
XXV	32.5	45	20	140,000	180,000	100,000
XXVIII	40	..	..	120,000		
XXIX	41	..	..	165,000		
XXXI	40	..	..	1[illegible]0,000		

The unitage presented as described on the manufacturer's label.

ened in the serum treated patients, owing to the frequent abrupt recovery shortly after the use of the serum. The serum treated patients did not receive sulfanilamide or sulfapyridine. The latter drugs were employed for some patients of the control series.

SUMMARY AND CONCLUSIONS

Concentrated and refined antipneumococcus rabbit serum is an efficient therapeutic agent in the type specific treatment of lobar pneumonia. This controlled study demonstrates the mortality rate of the non-serum treated patients four times that of the rabbit serum series. Sensitivity to the therapeutic rabbit serum is rarely encountered. It is remarkably free from immediate reactions and produces a relatively small percentage of thermal and delayed serum reactions. It lends itself to the concentrated single total dose administration, which procedure saves much time and probably enhances its therapeutic efficiency.

Cook County Hospital.

RENAL COMPLICATION IN SULFAPYRIDINE THERAPY

REPORT OF FIVE CASES WITH ONE DEATH

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In view of the rapidly increasing popularity in the use of sulfapyridine by the medical profession, it seems wise to report in detail five cases of hematuria, some of which were complicated with abdominal pain resembling that of renal or ureteral origin and one of which was complicated with uremia and was fatal. A special report by the Council on Pharmacy and Chemistry of the American Medical Association,[1] based on reports received from about 100 investigators, mentioned toxic renal manifestations of sulfapyridine as very rare cases in which there is temporary hematuria, which in some cases has been quite severe. In the same issue of THE JOURNAL three cases of hematuria, one presenting visible blood, occurring in association with the administration of sulfapyridine were reported by Southworth and Cooke[2] of New York. In two of their cases there were severe abdominal pain of renal and ureteral origin and nitrogen retention in the blood. Antopol and Robinson[3] reported formation of uroliths in the urinary tract of rats, rabbits and monkeys fed with sulfapyridine. Gross, Cooper and Lewis[4] produced urinary calculi containing 6.4 per cent sulfapyridine and 64.1 per cent acetylsulfapyridine in twenty-seven of thirty-nine rats by the administration of 1 Gm. of sulfapyridine per kilogram of body weight by mouth in two weeks or less. They also found that these urinary calculi caused death in some and varying degrees of renal damage in other animals by complete or partial urinary obstruction, with associated hematuria, pyelonephritis and nonprotein nitrogen, as well as retention of sulfapyridine. We are in accord with Southworth and Cooke that, as far as we can determine, there is no report of cases of renal complication in human beings other than the three they have reported and the four cases of gross hematuria, usually accompanied by ureteral pain, mentioned in a report of fifty cases of pneumococcic pneumonia by Graham,[5] nor have we seen any report of a death due to such renal complication.

REPORT OF CASES

CASE 1.—M. N. W., a girl aged 6 years, weighing 29 pounds (13 Kg.), was admitted April 3, 1939, with the chief complaint on admission of fever and cough of three days' duration. There was no history of former urinary disease. Routine

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All the sulfapyridine used in our hospital was prepared by Société Parisienne d'Expansion Chimique under the trade name "Dagenan." The chemical formula given is 2-(para-aminobenzene-sulfonamidepyridine).

1. Sulfapyridine, special report of the Council on Pharmacy and Chemistry, J. A. M. A. **112**: 1830 (May 6) 1939.
2. Southworth, Hamilton, and Cooke, Crispin: Hematuria, Abdominal Pain and Nitrogen Retention Associated with Sulfapyridine, J. A. M. A. **112**: 1820 (May 6) 1939.
3. Antopol William, and Robinson, H.: Urolithiasis and Renal Pathology After Oral Administration of 2-Sulfanilyl-Aminopyridine (Sulfapyridine), Proc. Soc. Exper. Biol. & Med. **40**: 428 (March) 1939.
4. Gross, Paul; Cooper, F. B., and Lewis, Marion: Urinary Calculi Caused by Sulfapyridine, Urol. & Cutan. Rev. **43**: 299 (May) 1939.
5. Graham, Duncan; Warner, W. P.; Dauphinee, J. A., and Dickson, R. C.: The Treatment of Pneumococcal Pneumonia with Dagenan, Canad. M. A. J. **40**: 325 (April 19) 1939.

examination of the urine showed a specific gravity of 1.021, a slight trace of albumin, pus cells 1 plus (about 5 to 10 per high power field), no erythrocytes, no casts and an alkaline reaction. Physical examination revealed coarse mucoid rales over both bases with diminished breath sounds and dulness over the left base posteriorly. Next morning there were more signs of localization of the lesion over the left lower lobe of the lung. Sulfapyridine was then started with 1 Gm. orally at 10 a. m. and 0.5 Gm. every four hours. The fever, which was around 102 to 104 F. after admission, dropped to normal within twenty-two hours after the treatment was begun and the lung signs began to clear. April 5 there was some vomiting and anorexia; sodium bicarbonate was given. April 6 at 6 a. m. (about forty-four hours after the initial dose of sulfapyridine) she passed grossly bloody urine. Gross hematuria was also present at 11 a. m. and 7 p. m. Urinalysis showed specific gravity 1.015, albumin 3 plus, no casts, few leukocytes (about 2 to 5 per high power field) and 4 plus erythrocytes. Coagulation time was 7.5 minutes and bleeding time was 1.5 minutes. A total of 7 Gm. of sulfapyridine had been given and was stopped immediately on detection of the hematuria. Fluid was forced and sodium bicarbonate was continued. The next day the urine specimen showed an alkaline reaction, a specific gravity of 1.015, no casts, no erythrocytes and leukocytes 1 plus. On the following day the urine was also essentially normal and no erythrocytes were found; the child was discharged April 10 without any sign of renal damage. A chemical analysis of the blood was not done.

CASE 2.—T. C. Y., a boy aged 7 years, weighing 30 pounds (13.6 Kg.), was admitted April 17, 1939, with the chief complaint of cough for three months and marked dyspnea for two weeks. Physical examination showed marked dyspnea and cyanosis, very dirty carious teeth and coarse and fine mucoid rales all over the chest. Clinical diagnosis was bronchopneumonia following pertussis. Routine urine examination showed a specific gravity of 1.026, alkaline reaction, no casts, no albumin, no erythrocytes and a few leukocytes. Pneumococcus type VI was isolated from the sputum. Sulfapyridine was started immediately with 1 Gm. followed by 0.5 Gm. every four hours for twenty-two doses, making a total dosage of 12 Gm. in about four days; 0.5 Gm. of sodium bicarbonate was given with each dose of sulfapyridine. Other medication included 7,000 international units of vitamin B and 16,000 international units of vitamin C during six days. On the evening of the 19th after about 7.5 Gm. of sulfapyridine (about fifty-four hours after the initial dose) blood was noted macroscopically in the urine, but this was not reported until two days later when there was already apparent improvement in redness of the urine, which had shown erythrocytes 4 plus the day before. The drug was immediately stopped after this report was received. One day after the sulfapyridine was stopped there was marked general improvement with return of appetite. April 24 the urine showed a specific gravity of 1.004, no albumin, no casts, only a few leukocytes and no erythrocytes. Improvement continued and the patient was discharged eighteen days later without any symptoms or signs of urinary trouble.

CASE 3.—C. A. S., a boy aged 8 years, weighing 40 pounds (18 Kg.), was admitted May 13, 1939, from a children's refugee camp with no history available. His chief complaint was anorexia of long duration. The temperature on admission was only 99 F. Physical examination was essentially negative. A locally prepared vitamin B solution and a dose of castor oil were given after admission while we were waiting for further observation. The temperature rose to 104.6 F. at 8 a. m. the next day; owing to congestion of the pharynx, sulfanilamide 0.18 Gm. three times a day was begun and given for one day. The specimen of urine taken while the patient was on sulfanilamide therapy revealed slight cloudiness, an acid reaction, a specific gravity of 1.020, few leukocytes, 4 mg. of ascorbic acid per hundred cubic centimeters of urine and no casts or erythrocytes. Examination of the blood revealed a leukocyte count of 5,500 with a differential count of 45.5 per cent of neutrophils, 48 per cent lymphocytes and 6.5 per cent monocytes. On the following day, because of detection of numerous mucoid rales in the base of the right lung, sulfapyridine was used instead of sulfanilamide. About forty-eight hours after the initial dose of the sulfapyridine and a total of from 6 to 6.5 Gm. of this drug having been given, slightly blood-tinged urine was noticed by the attending nurse, who, however, did not feel it important enough to inform the attending physician, since the dosage of the sulfapyridine had already been reduced. Next morning, after a total of 7.25 Gm. of sulfapyridine had been given, the patient passed about 150 cc. of markedly bloody urine, which on examination showed a specific gravity of 1.005, acid reaction to litmus paper, albumin 3 plus, leukocytes 1 plus, erythrocytes 4 plus and numerous unidentified crystals, which were described as long and slender and grouped mostly in bundles resembling uric acid or leucine crystals but not typical of either. Another 0.5 Gm. of sulfapyridine was allowed, though the fever had already returned to normal. After the 150 cc. of bloody urine, and during the entire next week until his death, he did not pass more than 80 cc. of urine. May 19, about ninety hours after the initial dose of sulfapyridine, the first convulsion occurred; another attack occurred during the night and another at 5 a. m. on the 20th. The blood pressure on that date was 122 systolic, 92 diastolic. With this picture acute glomerular nephritis after bronchopneumonia or chemical nephrosis was suspected. It was considered that this might be due to the administration of sulfapyridine, though no report of any such action of this drug has come to our attention. Very slight results as far as the urinary output and general condition were concerned were obtained with the often repeated intravenous dextrose therapy, and repeated dosage of 50 per cent magnesium sulfate, both orally and by retention enemas. Decapsulation of both kidneys was considered but not performed, because of the poor condition and risk of the patient. The patient complained of some abdominal pain but he did not make this clear after the occurrence of convulsions. Signs of congestion of the lungs were detected on the 23d, and the general condition of the patient rapidly declined. Chemical analysis of the blood showed nonprotein nitrogen 165 mg. and urea nitrogen 75 mg. per hundred cubic centimeters. The patient died of uremia and terminal bronchopneumonia on the 25th.

AUTOPSY PROTOCOL SUMMARY [6]

The body was well developed and moderately well nourished. The cranial vault was normal. The middle ears and mastoids presented only a small amount of mucoid secretion. The tympanic membranes were intact. There were no enlargements of the lymph nodes in the neck. The throat structures were normal. The thyroid was of normal gross appearance. The chest presented both pleural spaces clear and free of adhesions. The right lung revealed an apical peripheral lesion characteristic of a moderately advanced primary Ghon tuberculous infection. The rest of the lung revealed a moderate diffuse bronchopneumonia. The left lung presented a similar degree of bronchopneumonia but there was no tuberculous involvement. The hilar lymph nodes were enlarged, chiefly on the right, and revealed a moderate amount of caseation necrosis. The heart was of fairly good tone with mild right-sided dilatation, and the valves were normal. The peritoneum was clear. The mesenteric lymph nodes were somewhat enlarged and some presented caseation necrosis, especially those nearest the ileocecal area. The gastrointestinal tract presented tuberculous ulceration of the terminal ileum involving the ileocecal valvular ring. The spleen was slightly enlarged and of a moderate gray soft character. The liver was somewhat enlarged and of a dull mottled appearance on cut section. Microscopic section revealed peripheral small droplet fatty metamorphosis with moderate central congestion. The adrenals were congested and microscopically showed medullary hyperplasia of moderate degree.

The urinary system presented both kidneys slightly enlarged. Both capsules stripped readily, leaving smooth surfaces. The cortices were thickened and the cut surface showed moderate congestion. The pelves were slightly dilated and the pelvic mucosae were somewhat thickened, congested and hemorrhagic. Both ureters were dilated to a diameter of 8 mm. to the distal cystic portion. The mucosae of the ureters were likewise thickened, congested and hemorrhagic. The bladder was small

6. By Dr. C. L. Dale.

and contracted and contained a small amount of gray sandy particles. The right ureteral orifice protruded into the bladder in the form of a congested hemorrhagic papilla which would not admit a small probe either from the cystic side or from a slit made in the distal part of the ureter. There were a few small concretions in this part of the ureter of about 2 mm., grossly resembling "uric acid sand." The left ureteral opening did not project as a papilla but was moderately congested. A probe would not enter from the cystic side. On probing from a slit in the distal ureter a mass of concretion was found to plug the orifice effectually and only after its removal did the probe pass through. Unfortunately this sandlike material was lost in the fluids and was not examined for sulfapyridine. Miroscopic sections of the kidney revealed marked tubular dilatation both of the convoluted and of the collecting tubules. The glomeruli were enlarged and presented a compression of the capillary tufts, which appeared small and dark with a wide clear space between the tuft and Bowman's capsule. There was very little cellular reaction in the glomerular tufts. There were areas of marked congestion and hemorrhage in the medullary portions. Section of the pelves and ureters revealed marked congestion, edema and some hemorrhage, with a small amount of leukocytic infiltration, chiefly lymphocytes.

The cause of death was attributed to bronchopneumonia with uremia due to anuria caused by bilateral ureteral obstruction of the orifice.

CASE 4.—M. M. W., a girl aged 11 years, weighing 30 pounds, was readmitted May 27, 1939, after spending sixteen days in the isolation hospital with measles. For three days in our hospital her temperature fluctuated between 101 and 103 F., and bilateral myringotomy was done on May 29. Routine urinalysis showed slight cloudiness, alkaline reaction, albumin 2 plus, leukocytes 1 plus, no casts and no erythrocytes, and ascorbic acid 0.8 mg. per hundred cubic centimeters of urine. May 31 we decided to try sulfapyridine with an initial dose of 1 Gm. followed by 0.5 Gm. every four hours. The first was given at noon and the second dose at 4 p. m. The patient vomited and complained of some abdominal pain after the second dose. On the following morning she passed grossly bloody urine, which on examination showed an alkaline reaction, a specific gravity of 1.012, albumin 4 plus, erythrocytes 4 plus and no casts. Sulfapyridine was immediately stopped, a total of only 3.5 Gm. of the drug having been given. Sodium bicarbonate 0.3 Gm. every four hours was then given. The patient complained of severe abdominal pain and marked tenderness in the costovertebral angle on both sides. Her temperature dropped to normal during the night and rose to 99.6 F. the next morning. She vomited four times during that day and had definite oliguria. Fluids were forced and the gross hematuria gradually disappeared on the following day. Examination of the blood showed coagulation time 4.5 minutes, bleeding time 1 minute, platelet count 275,000 and fragility test with an initial hemolysis at 0.44 per cent and the complete hemolysis at 0.30 per cent, nonprotein nitrogen 31 mg. per hundred cubic centimeters, urea nitrogen 16 mg., uric acid 3.3 mg., creatinine 1.2 mg., chloride 460 mg. and calcium 12.1 mg. The next two days the alkali reserve of the blood was 70 mg. and 68.2 mg. per hundred cubic centimeters respectively. Streptococcus haemolyticus was isolated from the discharging ears. Sulfapyridine was given again after the patient showed no microscopic hematuria and had no more complaint of abdominal pain and tenderness. A total of 2.5 Gm. of sulfapyridine was given during the next twenty-four hours, but no hematuria was observed either macroscopically or microscopically. Sulfapyridine was then stopped but the temperature rose again to 102.6 F. and sulfapyridine was resumed with a total dosage of 3.25 Gm. spaced in forty-eight hours. Examinations of the urine were negative for the first forty-eight hours but showed erythrocytes 1 plus on the third day. Sulfanilamide was then substituted for sulfapyridine.

CASE 5.—M. M. Y., a girl aged 17 months, weighing 16 pounds (7.3 Kg.), was admitted May 24, 1939, with a history of diarrhea, cough and fever for two weeks following measles and marked dyspnea for the last two days. The clinical diagnosis was bronchopneumonia. Sulfapyridine was immediately started with 1 Gm. for the initial dose and 0.25 Gm. every four hours for sixteen doses and 0.125 Gm. every four hours for eighteen doses. May 30, sulfapyridine was stopped and chemical analysis of the blood showed nonprotein nitrogen 36 mg. per hundred cubic centimeters, uric acid 4.3 mg. and creatinine 1.2 mg. May 31, examination of the urine showed a few erythrocytes, a few leukocytes, an alkaline reaction and a trace of albumin, but the next specimen of urine was negative for erythrocytes. Two days after this sulfapyridine was again given for two days, intended for the patient's bilateral otitis media and an abscess; the specimen of urine taken right after sulfapyridine was stopped showed an acid reaction and 1 plus for erythrocytes.

COMMENT

We have treated a series of about forty patients with sulfapyridine in our pediatric department. The cause for such a high incidence of renal complication has not been determined; it is interesting, however, to note that most of our patients are suffering from general nutritional deficiency, dehydration and polyavitaminosis in addition to their chief complaint.[7] Whether or not this is sufficient to explain the frequent renal complication is not certain.

That hematuria may occur as early as within twenty hours after the initial dose of sulfapyridine (case 4) is remarkable. In three cases the hematuria occurred after forty-eight hours (cases 1, 2 and 3). Only in case 5 was it delayed for six days. Dosage does not seem to be an important factor in these cases. Ours was based on the age and is lower than that recommended by Barnett, Hartmann, Perley and Ruhoff;[8] in three cases it was 50 per cent higher than that (calculated on the basis of the patient's weight) recommended by Wilson and his colleagues,[9] in one case it corresponded to theirs and in the fatal case it was lower than theirs.

The autopsy definitely showed complete bilateral obstruction of the urinary tract by uroliths—the obstruction was in the terminal cystic portion of both ureters, and the patient died of uremia as the consequence of the complete obstruction. There were definite signs of recent acute dilatation of the upper urinary tract and petechial hemorrhages along the ureter and the renal pelves. We are induced to think that the hematuria in this case was the result of direct trauma on the urinary structures by the spiculated calculi and the backward pressure from the obstruction. Had we had this knowledge and suspicion when the patient began to suffer anuria and tried cystoscopic manipulation of the ureters or even emergency nephrostomy, the life of this patient might very well have been saved.

Our cases do not agree with the report on experimental animals by Gross and Cooper that the sulfapyridine calculi were associated with acid urine. Our cases showed that renal hematuria can occur in connection with both alkaline and acid urine in human beings. Sodium bicarbonate was given with the sulfapyridine in cases 1, 2 and 4, and the urine in these cases was alkaline. In case 5 hematuria occurred first with alkaline urine and recurred with acid urine on repetition of sulfapyridine therapy. In most of our cases in the pediatric department sodium bicarbonate was usually given with sulfapyridine; there occurred these five cases of renal hematuria with one death. On

7. This hospital admits only sick refugee Chinese, many of whom are living under very difficult circumstances such as are seldom if ever seen in the United States.

8. Barnett, H. L.; Hartmann, A. F.; Perley, Anne M., and Ruhoff, Mary B.: The Treatment of Pneumococcic Infections in Infants and Children with Sulfapyridine, J. A. M. A. **112**: 518 (Feb. 11) 1939.

9. Wilson, A. T.; Spreen, A. H.; Cooper, M. L.; Stevenson, F. E.; Cullen, G. E., and Mitchell, A. G.: Sulfapyridine in the Treatment of Pneumonia in Infancy and Childhood, J. A. M. A. **112**: 1435 (April 15) 1939.

the other hand, in the medical department of our hospital, where forty cases of adults were treated with sulfapyridine without sodium bicarbonate, there was not a single case of renal complication in the form of hematuria or any sign of urolithiasis. This suggests that children are more liable to renal complications with sulfapyridine medication; therefore, while this drug is administered, they should be very carefully watched and frequent examinations of the urine should be made for erythrocytes and sulfapyridine and acetylsulfapyridine crystals or stone formation.

SUMMARY

1. Five cases of hematuria were associated with administration of sulfapyridine in children.

2. One of these patients died of uremia as a result of bilateral complete urinary obstruction, proved at autopsy.

3. Hematuria may occur within twenty hours but may be delayed as long as six days after the initial dose of sulfapyridine.

4. The real mechanism of formation of the hematuria is still not known, but it may be associated with formation of uroliths.

5. Cystoscopic examination and ureteral manipulation and even emergency nephrostomy or renal pyelotomy with probing of the ureter for possible urinary obstruction by a competent urologist should be made when signs of marked urinary obstruction and anuria develop during the administration of sulfapyridine.

6. Children are probably more susceptible to renal complication in sulfapyridine medication and more care should be taken during its administration in pediatric cases.

37B Brenan Road.

Clinical Notes, Suggestions and New Instruments

A CASE OF WEIL'S DISEASE

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A condition characterized by sudden onset, prostration, fever, jaundice, muscular pains, hemorrhagic tendencies and renal involvement was first described by Weil [1] in 1886. In 1914 Inada was able to transmit this disease to guinea pigs by inoculating them with blood taken from patients suffering from this disease. The following year he [2] discovered that a spirochete was the etiologic agent. Noguchi [3] found that this organism differed from other spirochetes in that it did not have a terminal filament and that it was resistant to 10 per cent saponin and termed it Leptospira icterohaemorrhagiae.

Since 1922 about twenty-two cases of this disease have been reported in this country. We believe that our case is the first to be reported from New Jersey. Many authorities believe that this apparent rarity of the disease in the United States is due to failure to diagnose it rather than to scarcity of the disease. It is interesting to note that jaundice was a prominent feature in twenty-one out of twenty-two cases reported in America, although investigators in foreign countries find that about 50 per cent of their patients lack jaundice. One should therefore include Weil's disease in the differential diagnosis even when jaundice is absent but other symptoms are suggestive and call on the laboratory to confirm or reject one's suspicions. The following laboratory methods enable us to make a positive diagnosis of Weil's disease: guinea pig inoculation, darkfield examination, agglutination tests and tissue and smear staining.

Since Wolbach and Binger's [4] discovery in 1914, it has been known that natural waters of various kinds contain organisms which morphologically are similar to those which cause Weil's disease. However, these organisms are nonpathogenic and have been named Leptospira biflexa. There are several pathogenic strains of organism which morphologically resemble Leptospira icterohaemorrhagiae and cause such diseases as (*a*) swamp fever of eastern Europe, (*b*) akiyami or seven day fever of Japan and (*c*) a disease in dogs which resembles Weil's disease.

Weil's disease has been found throughout the world in locations where rats are present. Approximately 10 per cent of the rats in the world are infested with Leptospira icterohaemorrhagiae. Mice also frequently act as carriers. These animals carry the organisms in the tubules of the kidney, excreting them in the urine and thus inoculating water, soil or food with which they come in contact. Jorge [5] reports an epidemic in Lisbon in 1931 in which Leptospira was found in a public fountain. It was discovered that this water was contaminated by rat feces.

There are several ports of entry of the organisms into the body. The disease has followed cuts and needle pricks.[6] Infection by mouth has been produced experimentally and the Lisbon epidemic is an example of it. The disease was accidentally caused by spraying the infected material into the eyes of two laboratory workers.[7]

The period of incubation ranges between four and twenty days, usually from eight to twelve.

The principal pathologic changes in this disease are confined chiefly to capillaries, kidneys, liver and skeletal muscles together with generalized jaundice.[8]

Injury to capillaries is evidenced by the generalized hemorrhages in various tissues: subserous, mucosal, skin and brain, as well as parenchyma of liver, spleen, pancreas and the like. Capillary damage is sometimes very severe and is responsible for the epistaxis, hematemesis, hemoptysis and purpura. It is believed that the capillaries are damaged by the toxic action of the spirochetes.

Grossly the liver appears jaundiced and slightly enlarged. Microscopically the most common pathologic changes are hyperplasia of the liver cells, stasis in biliary capillaries toward the center of the lobule and some infiltration of portal spaces by leukocytes and lymphocytes.

The kidneys are usually slightly enlarged and jaundiced. Microscopically the most common pathologic changes are swelling and necrosis of the epithelium of convoluted tubules, and some infiltration of interstitial tubules by lymphocytes and to a lesser extent by leukocytes.

Very commonly calf muscles and less often other skeletal muscles present small hemorrhages and small areas of degeneration, which are infiltrated by several types of wandering cells.

Inada [9] recognized the fact that the clinical and pathologic features of the disease divided it into three stages: febrile, toxic and convalescent.

The First or Febrile Stage.—The disease usually begins with a chill, high fever and prostration. The more common symptoms are gastrointestinal disturbances, abdominal pain, conjunctivitis, herpes labialis, severe muscular pains and signs of

1. Weil, H. A.: Deutsches Arch. f. klin. Med. **39:** 209, 1886.
2. Inada, R.; Ido, Y.; Hoki, R.; Kaneko, R., and Ito, H.: J. Exper. Med. **23:** 377 (March) 1916.
3. Noguchi, Hideyo: J. Exper. Med. **27:** 575 (May) 1918.
4. Wolbach, S., and Binger, L.: J. M. Research **30:** 23, 1914.
5. Jorge, R.: Bull. Office internat. d'hyg. pub. **24:** 88 (Jan.) 1932.
6. Wadsworth, Augustus; Langworthy, H. Virginia; Stewart, F. Constance; Moore, Anna C., and Coleman, M. B.: Infectious Jaundice Occurring in New York State, J. A. M. A. **78:** 1120 (April 15) 1922.
7. Goebel, W.: Med. Klin. **12:** 381, 1916.
8. Dawson, B.; Hume, W. E., and Bedson, S. P.: Infective Jaundice, Brit. M. J. **2:** 345 (Sept. 15) 1917. Jeghers, H. J.; Houghton, J. D., and Foley, J. A.: Weil's Disease, Arch. Path. **20:** 447 (Sept.) 1935.
9. Inada, R.: J. Exper. Med. **26:** 355 (Sept.) 1917.

meningeal irritation. Examination of the blood shows a leukocyte count of between 10,000 and 20,000 and numerous spirochetes, but antibodies are lacking. Some degree of azotemia is present but the organisms cannot be found in the urine. This stage lasts from five to seven days.

The Second or Toxic Stage.—In about 50 per cent of the cases jaundice appears, and many cases show hemorrhagic tendencies. The liver is usually enlarged but the spleen is usually not palpable. Most of the symptoms of the first stage decrease in intensity and the temperature slowly falls to normal. Azotemia usually increases and there may be oliguria and even anuria. During this stage antibodies appear, spirochetes disappear from the blood and many organisms are excreted in the urine. This stage lasts from seven to ten days. When death occurs it is usually in this stage.

The Third or Convalescent Stage.—This stage is characterized by subsidence of the previous symptoms. In severe cases there is marked emaciation and anemia. In about one third of the cases there is another appearance of a low grade fever, which usually lasts from one to two weeks. Inada felt that this fever was due to disintegrating toxins caused by high serologic immunity. During this stage the organisms completely disappear from the blood stream and are excreted in the urine in large numbers. The serologic immunity is at its height during this stage.

REPORT OF CASE

G. W., a schoolboy aged 17, white, lives in a wooden shack with his mother and brother in Livingston, N. J. The patient's neighborhood is infested with rats—his home in particular. For several months preceding his illness he was in the habit of setting rat traps and removing the animals from the traps. He states that he was never bitten by any of the rats.

Except for the usual childhood diseases, the boy was in excellent health until Aug. 26, 1938. Late in the evening of that day he had a general malaise but nothing very definite. The following morning he was severely prostrated with severe headache, photophobia, congestion of the nose, sore throat, anorexia, nausea, stiffness and severe myalgic pains in the extremities, chilly sensations and fever, which soon rose to 104 F. That day he was seen by a local physician, who made a diagnosis of "grip" and treated the patient in the usual manner, including 10 grains (0.65 Gm.) of sulfanilamide. For the next several days these symptoms continued and the temperature ran high (from 104 to 105 F.). The physician saw the patient again on the morning of August 31. At that time he noted that, besides the siffness and painfulness of the extremities, the neck was stiff and Kernig's sign was positive. The room was darkened because of the patient's photophobia, making it impossible to see whether the patient was jaundiced. That day the boy was sent to St. Mary's Hospital in Orange, N. J., with the admitting diagnosis of meningitis.

On admission the patient presented a picture of severe prostration and deep jaundice. He wore dark spectacles because of the photophobia. He was conscious and oriented but mentally sluggish. He vomited almost continuously. The vomitus was scanty and blood stained. He objected to being moved in bed because of the pain which was produced in his extremities. His chief complaints were generalized pains, severe frontal headache, nausea and vomiting, photophobia and distress in the upper half of the abdomen. He stated that he had not urinated or defecated in the past four days.

More detailed examination showed the temperature 101.4, pulse rate 104, respiratory rate 24, blood pressure 110 systolic, 60 diastolic. His scleras were deeply jaundiced and there were extensive subconjunctival hemorrhages. The nasal mucosa was moderately congested. The lips were dry and the tongue had a heavy gray blood tinged coat. The pharynx was congested. The gums were a dark blue and spongy and bled slightly from the margins of the teeth. The breath was foul.

No adenopathy was found in the neck, which was, however, stiff and painful when the head was raised. The lungs were clear except for an occasional coarse rale. The heart percussed out within the normal boundaries, and its sounds were of fair quality. The abdomen was slightly distended and spastic throughout, especially in the right upper quadrant, where it was also quite tender. The patient complained that the abdomen felt "tight." The liver and spleen were not palpable. Distention of the bladder was not felt.

The extremities were generally stiff and tender and very painful on motion, pains being felt chiefly in the muscular regions, especially the calves. The reflexes were hyperactive. Kernig's sign was positive. Several hemorrhagic areas were found beneath the nails of the fingers.

The patient was unable to void, so that it was necessary to catheterize him to obtain a specimen of urine. About 100 cc. of dark, foul smelling urine was obtained. It showed 1+ albumin, a specific gravity of 1.020, sugar +—, several leukocytes per high power field, no casts and 4+ bile.

The blood count showed 7,900 leukocytes, 3,440,000 red cells and a 65 per cent hemoglobin content (Sahli).

The patient was given a low enema, which was productive of a small amount of tarry fecal material and a few small blood clots.

A lumbar puncture revealed the cerebrospinal fluid to be under increased pressure, but the cell count showed only three lymphocytes per cubic millimeter.

Two days after admission the chemical analysis of the blood showed sugar 125 mg., urea 90 mg., uric acid 10 mg. and creatinine 4.5 mg. per hundred cubic centimeters. The blood gave negative reaction to the Widal test. The Wassermann reaction of the blood was negative. The icterus index was 110. The van den Bergh reaction was positive, immediate and direct. The fragility test showed a slight decrease in the resistance of the red cells to hypotonic saline solution.

During the first few days in the hospital he was given intravenously a good amount of dextrose in saline solution. On his second day he received 500 cc. of citrated blood.

During the first week in the hospital his general condition was practically unchanged. The icterus index rose to 130 on the seventh hospital day. He lost considerable blood from frequent epistaxes. The temperature gradually reached normal after several days. The urine was very scanty and stained deeply with bile. Blood culture showed no growth. On the fourth hospital day a tender liver edge was felt two fingerbreadths and the spleen three fingerbreadths below the costal margin. His vomiting gradually decreased. The vomitus occasionally contained some dark bloody material. The stools were scanty, infrequent, tarry and occasionally mixed with some blood clots. He was given 300 cc. of citrated blood September 6. The following day his trunk and extremities were covered with a macular rash, which disappeared on pressure. This rash gradually grew scantier and finally receded after three days.

He appeared to be somewhat improved during the second hospital week. The icterus index descended to 75. He passed more urine, but the blood urea, uric acid and creatinine values remained unchanged. The photophobia and subconjunctival hemorrhages were still present. The pain and stiffness in the extremities were considerably decreased. The liver and spleen edges were barely palpable. The nausea and vomiting were practically gone and the patient was placed on a high carbohydrate liquid diet. Liver extract and iron were given intramuscularly daily, beginning the fourth day.

Several cubic centimeters of centrifuged urine was injected into a guinea pig subcutaneously and intraperitoneally on September 6. The pig died September 14.

Beginning with the eleventh hospital day and continuing for four days the patient's temperature was between 100 and 101 F. The blood count showed 18,200 leukocytes per cubic millimeter with 89 per cent polymorphonuclears.

During the third hospital week the patient's condition was definitely improved. The icterus index came down to 50. His eyes were clearing up and the photophobia was practically gone. The nausea and vomiting had disappeared and his appetite was slowly returning. He was given another 500 cc. of citrated

blood, and the liver and iron therapy was continued. Several hours before his last blood transfusion, a rash similar to the one described appeared and was accompanied by a moderate itching sensation. It disappeared gradually over a period of four days.

Chemical analysis of the blood September 21 showed urea 48 mg., uric acid 6.5 mg. and creatinine 3.7 mg. per hundred cubic centimeters. At this time his blood showed a hemoglobin content of 53 per cent, 2,930,000 erythrocytes and 11,850 leukocytes.

The fourth and fifth hospital weeks saw the patient's gradual recovery. The icterus index reached 28 September 27 and chemistry of the blood revealed urea 21 mg., uric acid 3 mg., and creatinine 1.5 mg. per hundred cubic centimeters. The jaundice in the scleras was very light and the subconjunctival hemorrhages had cleared. The stool was brown and the urine was only faintly bile stained. He was taking a soft diet very well. He regained sufficient strength to sit up in a chair and walk gently about his room. The hair on his head appeared very scanty and he had lost about 25 pounds (11.3 Kg.) during the illness. He was discharged from the hospital October 11.

On the seventh hospital day 60 cc. of catheterized urine was centrifuged and 4 cc. of the sediment urine was injected subcutaneously and intraperitoneally into a guinea pig. This pig died eight days later. The autopsy, performed by Dr. E. J. Tiffany at Long Island College of Medicine, revealed marked icterus of the scleras and subcutaneous tissues, subcutaneous and subperitoneal petechial hemorrhages, "butterfly-wing" mottling of the lungs, congestion of the kidneys and liver and a dark hemorrhagic appearance of the adrenals. These conditions are all characteristic of the reaction, in the guinea pig, to infection with Leptospira icterohaemorrhagiae. Morphologically typical leptospiras were found by darkfield examination in the pleural fluid, and in the liver and kidney pulp.

Dr. Tiffany injected organisms from this guinea pig into a second guinea pig. This pig had a temperature around 101 to 102 F. daily and finally 104 on the seventh day, when the pig appeared very ill. On this day he was killed. The autopsy showed conditions similar to those found in the first pig. Darkfield examination revealed the same organisms. The organisms from both guinea pigs were grown successfully on artificial culture mediums.

Stock cultures of Leptospira icterohaemorrhagiae were agglutinated by the patient's serum taken on the tenth day of the disease in a dilution of 1:320. Serum taken on the thirty-first day of the disease produced agglutination in a dilution of 1:20,000. Most of this laboratory work was done at Long Island College of Medicine.

Some of the patient's blood serum collected on the fifteenth day of the disease was sent to the U. S. Public Health Service at Washington, D. C. We received a reply that the serum from our patient agglutinated with their strain of Leptospira icterohaemorrhagiae in the high dilution of over 1:30,000. The reaction was prompt and clear cut and was, therefore, diagnostic for Weil's disease.

Workers from many parts of the world have reported successful results obtained by treating this disease with specific serum.[10] Animal and convalescent serums have been employed with almost equal success. Administration of serum produces an amelioration of the symptoms, a shortening of the duration of the disease and a marked decrease in the mortality rate. In this country the treatment is still symptomatic. The cases are so rare that it has been found impracticable to use the serum.

Inada [11] was able to produce marked reduction in the incidence of the disease in a certain Japanese locality by employing active immunization by means of vaccination. Vaccination is, however, impracticable in this country because of the low incidence of the disease.

135 South Centre Street.

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BACILLARY DYSENTERY

A PRELIMINARY REPORT STRESSING THE BLOOD PICTURE

H. M. GINSBURG, M.D.; EDWARD M. HIRSCHBERG, M.D., AND FLORENCE BRISKER, FRESNO, CALIF.

Dysentery, an acute intestinal infection, was known and described during the time of Hippocrates. From 1898 until 1916 various workers isolated organisms which bear their names and are said to be causative agents of bacillary dysentery. The etiology, pathology, symptomatology and treatment of bacillary dysentery have been adequately described and all writers apparently agree on the details.

In Fresno County an outbreak of dysentery is not uncommon each summer. The community is devoted primarily to farming and the migrant farmhands are numerous. They live in any type of shelter and the food that the family secures is not adequate or balanced. The unripe fruit is partaken of freely. The incidence of dysentery is more prevalent in children.

During the summer of 1937 we had occasion to admit to the General Hospital of Fresno County thirty-nine patients suffering from bacillary dysentery. Our attention was particularly attracted to these cases because of the similarity that existed in the reported blood counts. The admitting officer would not hesitate to diagnose dysentery of the bacillary type merely by viewing the blood count.

In nineteen, or 49 per cent, of the thirty-nine cases, culture of the stool was positive, in ten, or 25.5 per cent, it was negative and in ten a culture was not taken. There were twenty-three boys and sixteen girls. The ages of the patients varied from 3 months to 8 years, with an average of 2 years. The length of time that the diarrhea was present on admission varied from one to fourteen days, with an average of 4.4 days. The Flexner bacillus was the most common organism in the positive cultures. The average length of diarrhea was 14.2 days. The average length of the elevated temperature was thirteen days. There were ten deaths, or a 25.5 per cent mortality.

Routine blood counts were taken on admission and subsequent counts were taken as the patient's condition progressed while in the hospital. The white blood counts varied. Some patients had a normal count, others a high normal and the remaining an elevated count up to a maximum of about 30,000. The polymorphonuclear total was not significant but for the major part was elevated. The interesting fact to us was that all cases showed a Schilling differential count with a 95 to 100 per cent shift to the left. This was true in thirty-seven of the thirty-nine cases. Of the other two patients, one was a baby 3 months old and the diagnosis was not substantiated by all the pediatricians. The second case was of fourteen days' duration when first seen. Repeated counts on all patients showed that as the course of the disease progressed and as the temperature and diarrhea abated the Schilling count began showing the shift back to the right. This therefore may account for the second case not showing a 100 per cent shift, since the disease was abating when the patient was admitted. In cases of dysentery due to Endamoeba histolytica the white blood cell count is usually normal and no young forms are found in the differential smear. This finding was noted in all cases in which the laboratory reported a culture positive for histolytica. These cases of the bacillary type which showed a low white count in spite of the elevated polymorphonuclear cell count always showed an increased white cell count as the process progressed and as the Schilling count showed the shift back to the right.

The records for 1939 to date reveal twenty-one cases of dysentery, of which nineteen are due to the Flexner or the Sonne bacillus and two to Endamoeba histolytica. The Schilling count in the nineteen cases showed a shift to the left varying from 95 to 100 per cent. This count, as in those cases of 1937, shifts back to the right as the disease progresses. The two cases due to histolytica showed a normal Schilling distribution.

From the General Hospital of Fresno County.

The cases for 1939 will be studied further and at some future date a more comprehensive report will be made covering this subject.

CONCLUSIONS

1. We have attempted to present what we consider an interesting blood condition in cases of bacillary dysentery. We feel that it is possible to diagnose a case of dysentery as of the bacillary type if the Schilling count shows a 95 to 100 per cent shift to the left, except in those cases of long duration.

2. A further complete report will be made as soon as the 1939 cases can be fully studied. It is hoped that by that time other institutions in which dysentery is prevalent will be able to report on this condition.

Special Clinical Article

THE TREATMENT OF INSOMNIA

CLINICAL LECTURE AT ST. LOUIS SESSION

LOUIS J. KARNOSH, M.D.

CLEVELAND

Insomnia is a chronic inability to sleep. To the clinical mind the term connotes a condition in which an alleged sleeplessness is the main or solitary symptom, in which there are few tangible physical causes and in which the pathologic basis, if any, is not readily detectable. A person who has genuine pain and whose physical derangements are such that sleep is obviously impossible is not ordinarily regarded as having insomnia.

What constitutes true insomnia is largely a matter of capricious opinion on the part of both patient and physician. It would be of considerable advantage to determine whether there is a definite optimum of human sleep, that is, a basic requirement comparable to basal metabolism, from which deviations could be measured. Adult normal sleep defies standardization, for even the most regular of sleep rhythms must be regarded as a complex process which can be influenced by both physical and psychogenic excitations.

Basic sleep, if it exists, may be determined best by observing the spontaneous behavior in sleep of persons who live in a neutral atmosphere (if this is ever possible), whose routine is simple, who have little work to do and who are free from serious psychic impacts. In order to learn what constitutes an average sleep rhythm and to recognize what incidental factors modify such normal sleep, fifty women who had recovered from minor psychoses and who did not complain of insomnia were observed for three months in a psychiatric hospital. The optimum period of sleep varied from six and one-half to eight hours. No particular sleep curve was characteristic of any one patient. Age, temperament, menstruation, ovulation (determined by the so-called ovulation drop) and even diet were the endogenous factors correlated with the sleep curve. None of these consistently influenced the number of hours of sleep required. Perhaps the older patients showed a tendency to a little more sleep than the younger subjects and were prone to retire earlier and to get up earlier. Temperament may also have something to do with average sleep requirements, but the observations in this respect were indecisive. Possibly phlegmatic people require more sleep than those of a livelier and more labile disposition. Menstruation and ovulation made little or no impress on the sleep curve.

On the other hand, excitement incidental to visits by relatives, altercations with other patients or with attendants, and holidays, with their concomitant emotions, were definitely instrumental in breaking the normal sleep rhythm.

From these studies it is inferred that in the absence of grave organic disease the normal sleep rhythm is more vulnerable to psychic impacts than it is to the minor endogenous influences which are frequently credited with causing insomnia. Insomnia is prima facie a constitutional disorder in which psychopathologic phenomena play the leading part, although in some instances physical disorders can be revealed as contributing factors.

The person with insomnia often believes that persistent loss of sleep is a calamitous disturbance—a forebodement of death or insanity. Investigations which look into the effects of prolonged sleeplessness by no means tend to support such fears. Although complete deprivation of sleep in young experimental animals, as shown by Kleitman,[1] may prove lethal because of anemia, loss of weight and a collapse of the respiratory and temperature-regulating centers, no such baneful effects have been noted in the human being.

Kleitman[2] deprived himself of sleep for more than 100 consecutive hours. No anemia developed; neither was there a startling loss of weight. All bodily functions remained normal, and the ability to perform simple mental tests showed no change. Only steadiness in standing was much impaired. In other studies the same benign results were noted, except that some of the subjects experienced a marked, but temporary, ocular imbalance. Furthermore, what few stigmas appeared were readily abolished by a single period of sleep which was not greatly prolonged.

There is no good evidence that insomnia is a *bête noire* which saps one's vitality and health. It is doubtful whether, in the absence of grave physical signs, insomnia per se ever caused death. Gillespie[3] stated that he has yet to see a patient whose mental disorder could be fairly attributed to insomnia.

Reassurance of the patient is an important part of the treatment of insomnia, no matter what elements contribute to the disorder. The fact that insomnia, however extreme, has never been shown to be a dominant factor in the production of mental illness should be imparted to every person who suffers with sleep disorders. To some patients the possibilities are so dire that they dread bringing up the subject of impending insanity lest their worst fears be confirmed. Whether the patient introduces the subject or not, an open discussion and a proper assuagement may prevent a superimposed anxiety and contribute greatly to the abatement of the insomnia itself.

The person with insomnia frequently complains that his sleep is shallow and so fitful that it is not appreciated as sleep and that he arises in the morning unrefreshed, torpid and slow to acquire the mental acuity necessary for his day's work. The depth of sleep is

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From the Department of Nervous and Mental Diseases, Western Reserve University School of Medicine, and the Neuropsychiatric Division of the City Hospital.

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2. Kleitman, N.: Studies in the Physiology of Sleep: I. The Effects of Prolonged Sleeplessness on Man, Am. J. Physiol. **66**: 67, 1923.
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a matter of no little importance in any discussion of insomnia. It can be measured by the amount of stimulus required to awaken the sleeper. A popular method of studying the depth of sleep has been to record the movements of the patient, the assumption being that the fewer the movements the deeper the sleep. The actogram of Guttmann,[4] the hypnograph of Schiele[5] and the recording camera of Johnson and his associates[6] are all devices to obtain such data. In applying them in the case of insomnia, various results have been obtained as to the structure and quality of sleep. Important is the fairly consistent observation that the patient's own estimate as to the amount of sleep he enjoys is less than that obtained from the nurses' observations and decidedly less than that recorded by the mechanical device.

Since there is good reason to believe that most persons with insomnia exaggerate the degree of their sleeplessness, the physician should be aware of this propensity to overpaint the picture and should not be guided by the subjective data in his therapeutic approach. Shallow, fitful sleep may not be satisfactory but is often a natural condition compatible with the temperament and living habits of the individual patient and does not necessarily call for special attention or treatment.

Insomnia's favorite attack is on the very early hours of sleep, the "temps latent" of Ladame,[7] which is the time between retiring and of actually going to sleep. During this interval even the normal person experiences a certain twilight state. With the muscles gradually relaxing and the eyes closed, various imaginal mechanisms come into consciousness. They consist of a panorama of loosely connected and untrammeled ideas which may, among other things, contain a review of the day's events and plans for the morrow, gradually giving way to disjointed fantasies, which are fragments of experiences both remote and recent. Characteristic of this fantasmagoria is the absence of a dominating concept or theme; there seems to be no ability to hold to one particular fantasm and to reject others. Willy-nilly the thoughts pass in and out of consciousness without cohesion or regulation. Such loose linkage of ideas is called free association, and psychopathologists look on this mental rambling as an overture to sleep, in fact a half sleep wherein the higher cerebral functions which regulate logical and coherent thinking are at rest.

The person with insomnia dreads this phase of his sleep troubles. The period of free association torments him, for it may last several hours. He attains the portals of sleep but seems to have trouble getting any further. Moreover, the panorama is generally fearful and morbid, and its contents, although disconnected, frequently disclose the general source of anxiety. One of the immediate causes of insomnia is an anxious preoccupation, such as great concern over health, the repercussion of bitter family scenes, reflection on sexual inadequacy or infidelity, contemplation of business reverses and various other frustrations of the ego. These elements come and go despite the desire to forget them. As a matter of fact, the person with insomnia tries to forget them and in so doing makes matters worse, for he merely represses them and the effort keeps him from sleeping.

The sufferer may resort to such devices as counting sheep, reading in bed and other mental gymnastics that require concerted thinking. These are merely tricks for the further repression of unpleasant ideas and therefore actually lead the patient away from, rather than toward, sleep. The person with insomnia should be told to lie down, to let his muscles relax if he can, to let his thoughts wander where they will and to avoid the exercise of any sort of concentration or volition. No one can will himself to sleep; one merely allows sleep to intervene. He should be informed with regard to the phenomena of free association. If free association is a morbid and anxious experience, it is so because the patient has problems which should be cleared up in his waking hours. He must not use them as bedfellows.

Muscular relaxation is an essential precondition of sleep and was particularly emphasized by Kleitman. In the nervous person with insomnia, this is often as difficult to attain as is sleep itself. The only radical method for inducing bodily relaxation is the relief of the anxiety, but there are useful adjuvants. A good bed and a quiet room are obviously important. The bath is useful in reducing muscle tone but is not uniformly helpful. From fifteen to twenty minutes in a tub of water which is just cool to the touch is recommended if it does not upset the patient. Hot baths and massage are of questionable value.

Many sleepless patients resist the temptation to take an afternoon nap because they fear that they will not sleep so readily at night. There is no foundation for this fear. On the contrary, a moderate amount of diurnal sleep is beneficial; it teaches relaxation and engenders confidence in the person with insomnia for it demonstrates that he is capable of genuine sleep.

Nearly one half of all persons with chronic insomnia belong in the psychoneurotic category. The psychoneurotic patient emphasizes his need of sleep because sleep offers him a respite from his psychic conflicts. He not only wants sleep—he wants oblivion. He entertains the naive hope that after a night's good rest he may awake free from tension and depression and that the medication will wash away the problems which he is unable to face and solve. The psychoneurotic patient artfully presents his insomnia as a red herring across the path of the clinician's speculations to mislead him into believing that the trouble is a somatic one which merits medical treatment.

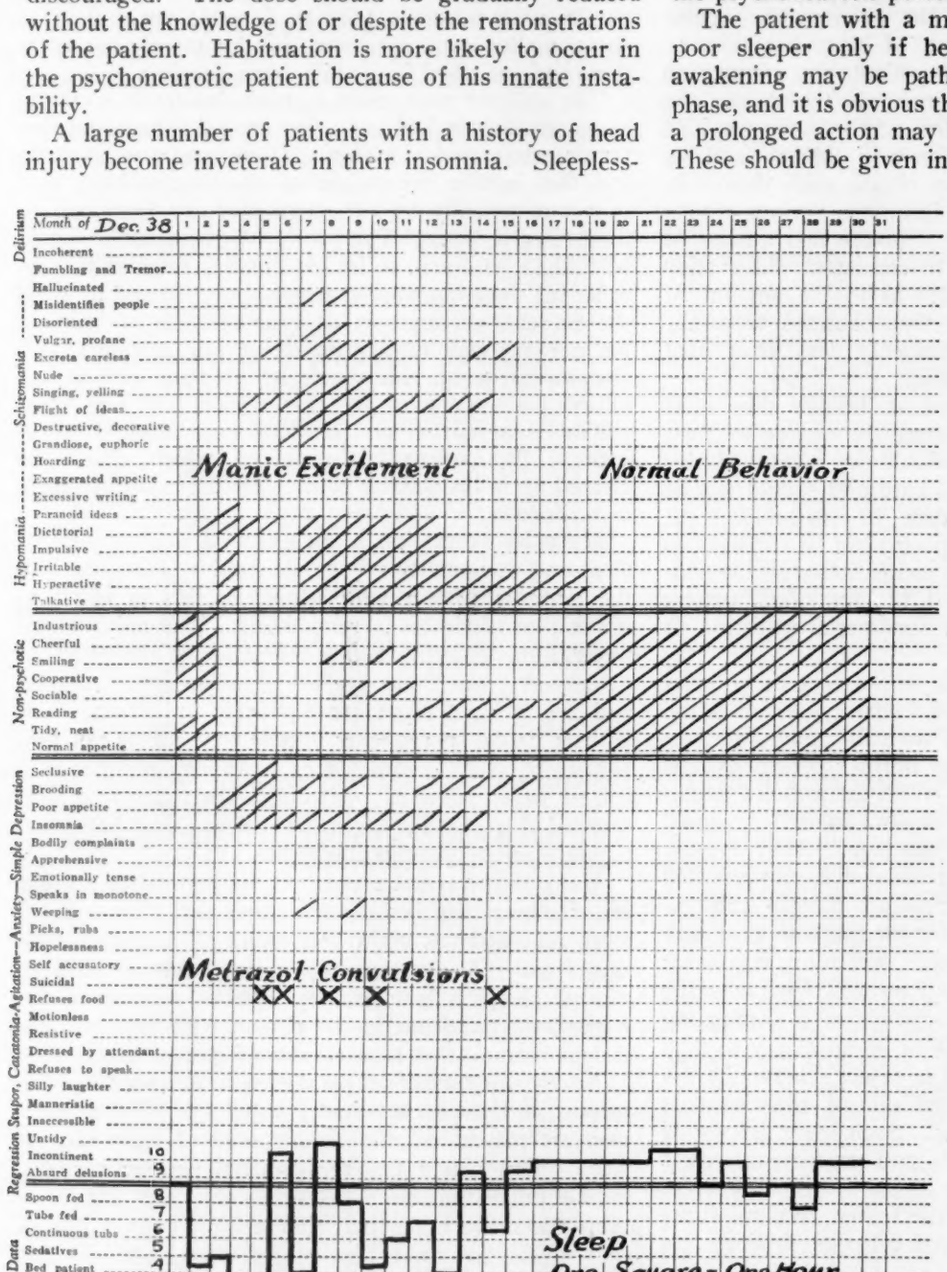
It is clear that the first and only satisfactory method of treating sleeplessness in the psychoneurotic states is to remove the source of psychologic tension. A mental aeration is far more valuable than a sedative. Sedatives should be regarded only as an adjunct, not as a device to cover up the fundamental difficulty. Only agents which act speedily and act intensely for a sufficient time to cover up the period of anxious preoccupation and to initiate sleep are indicated. The newer barbiturates, which are rapidly disintegrated, are particularly useful. One full therapeutic dose should be given at bedtime. The patient should not be preoccupied with the promise of additional doses if the first one fails, and morbid

4. Guttmann, E.: Actogramme als klinische Schlafkontrolle, Ztschr. f. d. ges. Neurol. u. Psychiat. **111**: 309, 1927.
5. Schiele, B. C.: Clinical Studies with the Hypnograph, Tr. Central Neuro-Psychiatric A., Minneapolis, Oct. 7, 1938.
6. Johnson, H. M.; Swan, T. H., and Weigand, G. E.: In What Position Do Healthy People Sleep? J. A. M. A. **94**: 2058 (June 28) 1930.
7. Ladame, C. H.: Du sommeil et de quelques-unes des ses modalites chez les aliénés, Schweiz. Arch. f. Neurol. u. Psychiat. **13**: 371, 1923.

curiosity as to the kind of sedative given should be discouraged. The dose should be gradually reduced without the knowledge of or despite the remonstrations of the patient. Habituation is more likely to occur in the psychoneurotic patient because of his innate instability.

A large number of patients with a history of head injury become inveterate in their insomnia. Sleeplessness is associated with vague headaches, a peculiar form of dizziness, head noises and inability to concentrate. This so-called headwound syndrome is rarely accompanied by objective signs of organic defect and appears after both trivial and severe trauma to the cranial contents. Although true anatomic change cannot be absolutely eliminated, in general the symptoms resemble those of the psychoneurotic patient who has had no head injury. The belief that the trouble is mainly a psychoneurosis is supported by the fact that many of the patients are involved in controversies over monetary compensation and the insomnia is not infrequently cured when a satisfactory settlement is made. The treatment should be mainly that which is applicable to the psychoneurotic person.

The patient with a manic-depressive psychosis is a poor sleeper only if he is agitated. Early morning awakening may be pathognomonic of the depressive phase, and it is obvious that the hypnotics which possess a prolonged action may be administered to advantage. These should be given in adequate doses and may even be administered to the extent that continuous narcosis is produced.



BEHAVIOR CHART

Chart 1.—The abatement of wild excitement and erratic sleep behavior in a young manic patient after five metrazol convulsions.

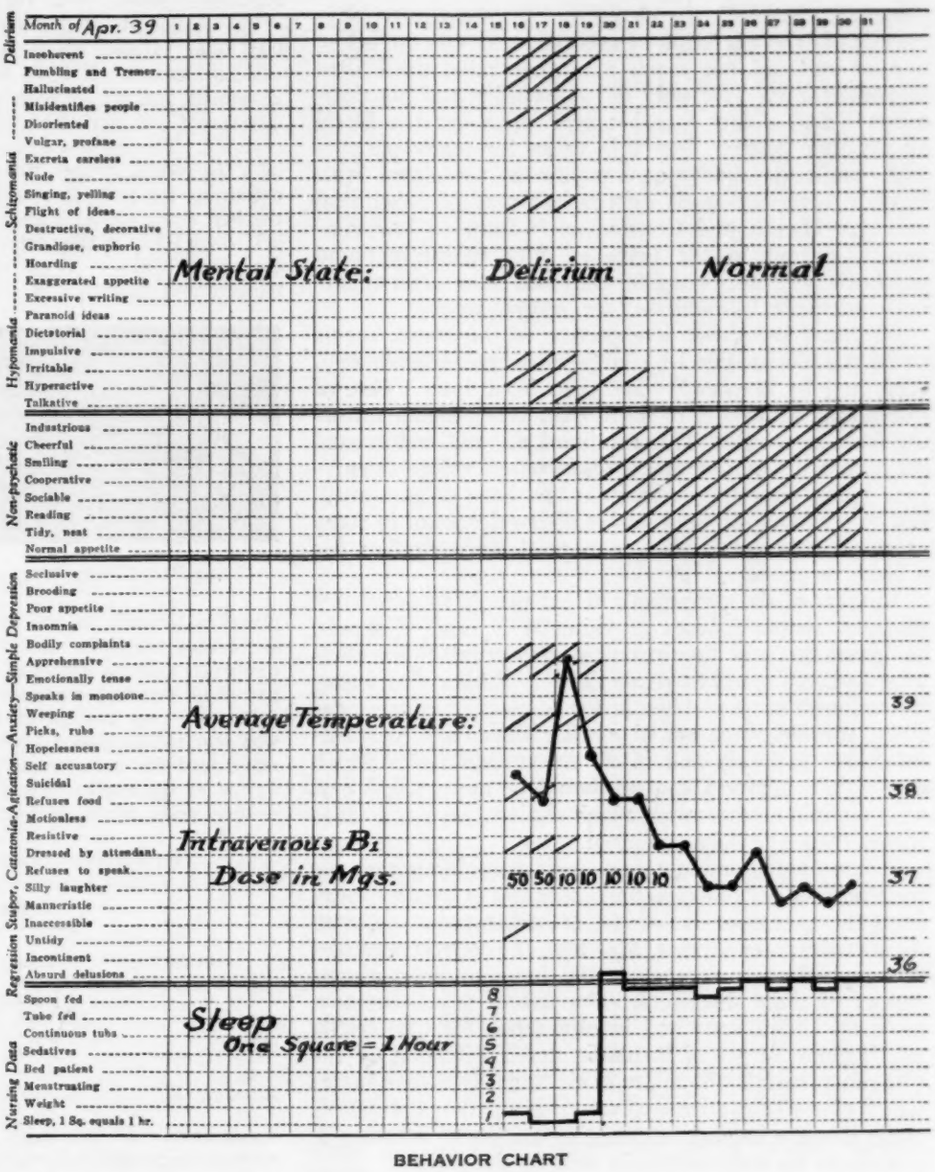
An extremely trying ordeal is the nocturnal excitement and sleeplessness of the manic phase, particularly in the younger person. The use of the continuous tub and prolonged narcosis have both proved to be unsatisfactory not only because of the irregular results but because of the danger of vasomotor collapse. Paradoxically, the most efficient agent is the metrazol convulsion. The administration of metrazol so modifies the behavior of the manic patient that after three or four convulsions the mood often returns to normal and concomitantly normal sleep is reestablished (chart 1). Eight manic patients and one depressed patient with insomnia and agitation were treated in this fashion with gratifying results. Moreover, in six other cases of depression and in one case of mania in which insomnia was not present the use of this convulsing drug did not interfere with the normal sleep cycle. Although one must give grave consideration to the recent disconcerting reports of Polatin, Friedman, Harris and Horwitz [8] to the effect that the metrazol convulsion frequently causes compression fractures of the vertebrae as well as dislocations, it appears that no other measure can quell the excitement of the manic phase or the agitation of the patient with melancholia in the same effective manner as this admittedly radical technic.

Almost as difficult to control as the insomnia of the manic phase is the excitement of the young schizophrenic patient, although in schizophrenia sleep is not consistently disturbed. Sedatives have a very unsatisfactory and irregular influence, particularly on catatonic excitement. The insulin shock technic yields better and more lasting results. Although during the course of

8. Polatin, Phillip; Friedman, M. M.; Harris, M. M., and Horwitz, W. A.: Vertebral Fractures Produced by Metrazol-Induced Convulsions, J. A. M. A. **112**: 1684 (April 29) 1939.

the treatment there may be some difficulty in producing adequate sleep, within a few weeks the schizophrenic patient sleeps normally every night, and this may often occur even before the mental picture itself shows any evidence of improvement. While the insulin shock may be a heroic form of treatment, in the long run it is no more noxious than the cumulative effects brought about by the frequent use of the various barbiturates and bromide salts. Schizophrenia is always a grave clinical problem and every aspect of it merits a formidable therapy.

Toxic states are a frequent cause of sleeplessness, particularly those induced by the excessive use of such stimulants as coffee, amphetamine or alcohol. Of the first two little need be said, for the treatment is obvious. It is a little absurd to talk of insomnia in extreme alcoholic intoxication, when the sensorium is completely clouded and many of the vegetative functions are badly deranged. Nonetheless, the confusion, the tremor and the nocturnal excitement call for more than ordinary measures to combat the psychic unrest. The routine as recently outlined by Bowman, Wortis and Keiser [9] has been the therapeutic procedure of choice of most clinicians. This consists of abrupt withdrawal of alcohol and judicious use of sedatives, with a preference for paraldehyde and a condemnation of morphine. Sodium chloride is administered to combat dehydration, and a high calory, high vitamin diet is provided. However useful this program may be in cutting down the mortality rate, the sleeplessness of acute alcoholic intoxication does not improve until the patient is well into convalescence.



BEHAVIOR CHART

Chart 2.—The dramatic response to vitamin B1 therapy, particularly with reference to sleep, of an acute alcoholic delirium.

Much more effective is the intravenous use of crystalline vitamin B_1. In nine cases of acute delirium the entire picture of confusion and tremorous excitement was dramatically terminated within five or six days (chart 2). Even more enthusiastic results were reported by Kloster,[10] who gave vitamin B_1 to ten patients in whom delirium tremens had not yet completely developed. One or two hours after the injection of one 50 mg. dose, a surprising improvement was noticeable, and eight of his patients slept quietly the first night. In our own experience with ten patients, normal sleep returned within a maximum of eight days and only one patient died, his condition having been complicated by osteomyelitis. It is believed that such results are not merely a happy fortuity, and today vitamin B_1 should be looked on as the perfect sedative for delirium tremens. Fifty mg. given intravenously once a day for three or four successive days is the dose recommended. The only undesirable side effect appears to be a tendency to hypertension.

The use of vitamin principles is not only beneficial in treating alcoholism but is of advantage in treating many other toxic-exhaustive states, such as hyperthyroidism. The patient with thyrotoxicosis is notoriously a light sleeper but may not always offer this as a primary complaint. Frazier and his fellow workers [11] supplemented the routine preoperative preparation of hyperthyroid patients with the hypodermic injection of 10 mg. of crystalline vitamin B_1 every other day and

9. Bowman, K. M.; Wortis, Herman, and Keiser, Sylvan: The Treatment of Delirium Tremens, J. A. M. A. **112:** 1217 (April 1) 1939.
10. Kloster, J.: Treatment with Vitamin B1 in Delirium Tremens, Nervenarzt **11:** 413 (Aug. 15) 1938.
11. Frazier, W. D., and Ravdin, I. S.: Use of Vitamin B1 in Preoperative Preparation of Hyperthyroid Patients, Surergy **4:** 680 (Nov.) 1938.

the oral administration of 10 Gm. of brewers' yeast every day. Compared with a control group, which was treated with compound solution of iodine alone, the vitamin-treated patients showed a slower pulse rate and a better appetite and gained weight to such a degree that they were more quickly and adequately prepared for operation.

A serious rival of vitamin B_1 as an ideal sedative in exhaustive states may be ascorbic acid, the vitamin C principle. Lewis [12] discovered that in preoperative thyrotoxicosis the excretion of ascorbic acid was far below normal and did not reach a normal value until after thyroidectomy. Not only did Alexander and his associates [13] find a low ascorbic acid value for the blood of alcoholic addicts, but this value for many patients with senile psychoses and psychoses associated with cerebral arteriosclerosis approached that of subclinical scurvy. Minski and Constantine [14] found a low vitamin C output in the urine of fifty undifferentiated psychotic patients, even after they had been on an apparently adequate hospital diet for several weeks.

Ordinary insomnia, irrespective of the cause, seems to be readily modified by large doses of ascorbic acid, according to Maurer.[15] He gave from 1 to 3 Gm. of l-cevitamic acid daily to more than 100 patients suffering from insomnia. This produced a sound and normal sleep, and the major effects disappeared within twenty-four hours after the medication had been discontinued, not only leaving no undesirable after-effects but in some cases actually establishing a normal sleep rhythm for a week or more.

In view of the propensity of old people to deficiency diseases, massive doses of vitamins B_1 and C should be given to stay the insomnia incidental to cerebral arteriosclerosis and to senile decay. Rather than being treated with large and continued doses of ordinary sedatives, the sleeplessness of cardiac deficiency, of post-infectious cachexia and of all exhaustion states which deplete the nervous system should be approached first with vitamin replacement, which obviously treats a cause rather than a surface symptom.

It is a fine commentary on modern medicine that the treatment of nervousness and insomnia is veering away from the excessive use of the orthodox sedatives, with their toxic potentialities, and that the newer therapies are applied with an eye on the basic or fundamental causes of these disorders. The use of psychotherapy, metrazol convulsions and insulin shock for the strictly psychogenic forms of insomnia and application of the vitamin principles to many toxic and exhaustive states which give rise to abnormal unrest are perhaps prophetic signs that the heyday of drugging and mere masking of symptoms by stupefaction is well on the wane.

12. Lewis, R. A.: Effect of Hyperthyroidism on Vitamin C, Bull. Johns Hopkins Hosp. **63:** 31 (July) 1938.
13. Alexander, Leo; Pijoan, Michel; Schube, P. G., and Moore, Merrill: Cevitamic Acid Content of Blood Plasma in Alcoholic Psychoses, Arch. Neurol. & Psychiat. **40:** 58 (July) 1938.
14. Minski, L., and Constantine, N. D.: Estimation of Vitamin C Content of Urine of Fifty Patients Suffering from Psychoses, J. Ment. Sc. **84:** 541 (May-July) 1938.
15. Maurer, S.; Wiles, H. O.; Schoeffel, E. W., and Fisher, M. L.: Effect of l-Cevitamic Acid in Insomnia: Preliminary Report, Illinois M. J. **74:** 971 (July) 1938.

Maintenance Diets.—A maintenance diet is one which contains that quantity of nourishment which will maintain the body at its ideal weight; it is the key to the dietetic treatment of obesity because it is the basis from which reducing diets are formulated; success or failure of the latter depends on the correctness or otherwise of the maintenance estimate.—Christie, W. F.: Ideal Weight: A Practical Handbook for Patients, London, William Heinemann, 1938.

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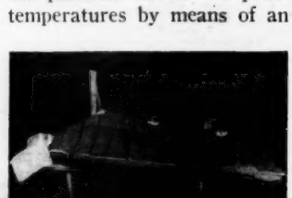
HOLLAND-RANTOS FEVER BAG ACCEPTABLE

Manufacturer: The Holland-Rantos Company, Inc., 37 East Eighteenth Street, New York.

The Holland-Rantos Fever Bag is intended to prevent heat loss from patients whose temperature has been elevated by various methods. It is 76 by 36 inches in size, weighs about 25 pounds, and is filled with kapok between a rubber-calendered, waterproof and sterilizable lining and a waterproof drill outer covering. The top of the bag may be raised in a tentlike fashion by a bar passed through rings and suspended from the bed, thus permitting the patient some mobility. One slide fastener closes the bag along one side and across the bottom; another closes a U-shaped flap in the center, intended to facilitate attending to the patient's needs. A provision is afforded for taking rectal temperatures by means of an 18 inch opening tied by tapes at the left center. A Russian-style collar may be adjusted to neck size.



Holland-Rantos Fever Bag.

In order to provide evidence for the maintenance of heat by the unit, the firm submitted twelve fever charts from a competent investigator who used this bag in conjunction with an acceptable short wave apparatus to produce the initial heat. The heat was applied by means of a cable from the short wave unit placed underneath the bag and separated from it by two layers of turkish toweling. Some of the same patients were also treated in cabinets energized by electric lights and short wave, and they reported comparable feelings in the two types of apparatus. An average of two hours and thirty-five minutes was required to induce a temperature of 106 F., and this was maintained for an average of four hours and thirty minutes. In ten of the twelve tests the short wave unit was used four or five times during each treatment in order to maintain the temperature. In two cases the fever was held above 106 F. after a single application of short wave diathermy.

Temperatures Summarized from the Charts

	Heat Induction		Heat Maintenance	
Chart No.	Time	Temperature at End, F.	Time	Temperature Range, F.
1	3′ 30″	106.0	4′ 30″	106.0-106.2
2	2′ 30″	104.6	5′	104.6-105.5
3	45″	102.4	5′	102.4-104.6
4	2′ 15″	105.8	4′	105.8-107.0
5	1′ 15″	104.8	4′ 45″	104.8-105.8
6	2′ 35″	105.6	4′	105.6-106.8

From the charts submitted it is observed that the temperature in the bag rose gradually as the rectal temperature did but never rose to as high levels as those of the rectal or cutaneous temperatures. The temperature of the skin did not rise above 103.5 F. Between the head and the foot ends of the bag, temperature differences of 2 degrees F. were noted at times. The humidity in the bag was about 100 per cent. There were no evidences of cutaneous burns, and the blood pressures, pulse rates and respiratory rates were similar to those in other methods of physically induced fever. No evidence of delirium was shown.

The firm also submitted two charts from another physician who used the bag. In an electric cabinet the temperature of one patient was raised to 106.2 F. in about three hours. Then the patient was transferred to the bag, and the temperature was maintained between 105.4 and 107.2 F. for about six hours, after which it fell steeply to 102 F. in the subsequent four hours in the bag. In the other case the fever was generated through

the bag by an electric induction apparatus. One hour and forty minutes was necessary to raise the patient's temperature to 106 F. in the bag and it was maintained between 105 and 106 F. for about five hours with the aid of hot water bottles.

Six other charts were also submitted from a hospital for the firm, giving data on the use of the bag with short wave apparatus to induce fever.

In the first and fourth charts it is to be noted that, one hour after the first application time, short wave was applied a second time for thirty minutes. It is also to be noted that an average of 1.1 degrees F. was gained at various intervals after turning off the short wave current and leaving the patient in the bag. In two of the charts the pulse rate increased continually until the end of the treatment.

The unit was investigated clinically for the Council. The induction period is a little longer than necessary when the bag is used with short wave diathermy, and patients are not as comfortable in the bag as in a cabinet, although, when the bag is so arranged that the top portion is lifted away from the patient by means of the special attachments, patients are not so uncomfortable as in types of cloth bags not so equipped.

In the opinion of the Council, this type of slide fastener bag is as satisfactory as any type of fever bag in affording a means of insulation, but it is still inferior to acceptable cabinets now on the market recommended for the same use.

The device may be used for maintaining the temperature of patients whose fever has been induced by hot baths or by other means when the temperature is not raised above 104 F. and when the length of treatment is not over four hours.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Holland-Rantos Fever Bag for inclusion in its list of accepted devices.

WESTINGHOUSE MODEL 250 SHORT WAVE ENDOTHERM ACCEPTABLE

Manufacturer: Westinghouse X-Ray Company, Inc., Long Island City, N. Y.

The Westinghouse Model 250 Short Wave Endotherm is intended for routine office practice in medical and minor surgical procedures. It is a portable model which may be obtained with a subcabinet. Cuff, pad and cable electrodes and felt spacers are part of the standard equipment. Surgical accessories and orificial electrodes are also available. The instrument panel has two separate controls, one for pad, cuff and surgery and one for the coil technic. There is a meter, serving as a combination milliameter and voltmeter. A forced draft ventilating fan is in the cabinet.

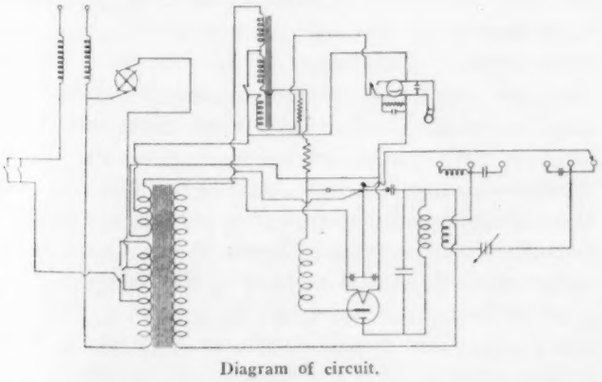


Diagram of circuit.

One tube is employed in a tuned-plate, tuned-grid circuit. The wavelength is 22.4 meters. Both the cable and pad circuits are inductively coupled.

The manufacturer claimed that when measuring with the photronic cell and lamp load method and with an input of 720 watts there is an output of 275 watts. In the calorimeter method, with two and one-half turns of the cable immersed in a 0.3 per cent salt solution and an input of about 740 watts, the output measured was 284 watts.

In the laboratories serving the Council, with the photronic cell and lampload method, the power input under a full load showed a maximum of 735 watts and an output of 292 watts. When the cable was used with three and one-half turns, a maximum input of 670 watts, the output on a calorimeter was 272 watts. After two hours' continuous operation at an input of 735 watts, the temperature rise in the outside windings of the transformer was 83 C. Although the tests made by the Council and the firm differed in certain details, they were sufficiently similar to substantiate in general the claims made by the firm on the physical performance of the apparatus.

RESULTS OF TESTS

In order to provide evidence for the tissue-heating power of the unit, the firm submitted the data collected by a qualified investigator:

Cuff Technic.—Two cuff electrodes with approximately 0.5 inch spacer under each were wrapped around the thigh with approximately 4 inches spacing between the proximal edges.

Average Temperatures of Six Observations after Twenty Minutes' Application

Deep Muscle, Degrees F.		Oral, Degrees F.	
Initial	Final	Initial	Final
97.8	104.7	98.7	98.9

Average Temperatures of Six Observations After Twenty Minutes' Application

Deep Muscle, Degrees F.		Oral, Degrees F.	
Initial	Final	Initial	Final
96.8	105.3	98.1	98.4

Average Temperatures of Six Observations After Twenty Minutes' Application

Deep Muscle, Degrees F.		Oral, Degrees F.	
Initial	Final	Initial	Final
97.1	103.8	98.4	98.6

Average Temperatures of Six Observations

Minutes	5	10	20	30
Degrees F.	101.5	106.8	107.3	109.8

The thermocouples were inserted to the full depth of the cannula and the skin temperatures were recorded at a point adjacent to the place where the incision had been made. All treatments were given to the patient's tolerance.

Inductance Cable Technic.—Four turns of the inductance cable were made around the thigh with approximately one-half inch turkish toweling beneath for spacing. Two turns were made high up on the thigh, where approximately 3 to 4 inch spacing was allowed to provide for inserting the thermocouples; then two more turns were taken below the incision.

Treatment Drum Technic.—The treatment drum was applied over the thigh as close to the skin and as nearly over the point where the temperatures were read as the inserted thermocouples would permit.

Orificial Tests.—A large Chapman electrode was used, drilled to pass a thermometer to allow a mercury bulb to come in contact with the cervical tissues.

A large short wave pad was used as the indifferent or dispersive electrode and connected to the No. 1 pad terminal of the machine. This was placed over the lower part of the abdomen separated from the skin by approximately 3 inches of folded turkish toweling.

The Chapman electrode was connected by a standard 42 inch lead to the No. 3 pad terminal and inserted into the vagina. The thermometer was inserted to contact the cervix and left in position throughout the treatment.

The unit was placed in a clinic, where it was found to operate satisfactorily and to provide ample heating for routine clinical work.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Westinghouse Model 250 Short Wave Endotherm for inclusion in its list of accepted devices.

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SATURDAY, SEPTEMBER 30, 1939

THE PROGNOSIS IN SUBACUTE BACTERIAL ENDOCARDITIS

Subacute bacterial endocarditis has for many years been considered practically incurable. A recent review [1] of eighty-eight cases observed at the Wisconsin General Hospital indicated the occurrence of only one healed case. The septic type of subacute bacterial endocarditis, almost invariably fatal, has become so familiar that the group of patients with a mild degree of infection in which there is a chance of recovery has been overlooked. Perhaps the time has come to change the conventional view of this disease.

Capps [2] has recently reported a study of 139 cases, all followed over a long period of years or to the fatal outcome. Thus one patient, whose condition was first diagnosed in 1910, is today in good health. Eleven patients survived five years or more after the onset of the infection. Included among the recoveries are only those patients who have remained symptom free for more than five years. The guilty organism in all of the cases reported by Capps over a period of twenty-eight years was Streptococcus viridans. There were heart murmurs, fever and blood cultures yielding the streptococcus in all these cases, and often embolic phenomena. Some early reports of recovery from subacute bacterial endocarditis were viewed with skepticism; they presented unsatisfactory proof of a correct diagnosis, and some patients had survived so short a time that the appearance of recovery might be interpreted as a remission. There are, however, more authentic reports of recovery. Conspicuous is the report by Oille, Graham and Detweiler,[3] who in a short period discovered twenty-three cases of a benign form of subacute bacterial endocarditis, and ten years later at least twenty of them were living. Libman [4] has studied some of these remarkable cases. Capps tabulates other reports of recovery in his review.

1. Middleton, William S., and Burke, Mead: Streptococcus Viridans Endocarditis Lenta, Am. J. M. Sc. **198**: 301 (Sept.) 1939.
2. Capps, Joseph A.: Subacute Bacterial Endocarditis Due to Streptococcus Viridans, with Special Reference to Prognosis, Ann. Int. Med. **13**: 280 (Aug.) 1939.
3. Oille, J. A.; Graham, Donald, and Detweiler, H. K.: Tr. A. Am. Physicians **39**: 227, 1924.
4. Libman, Emanuel: Tr. A. Am. Physicians **40**: 351, 1925.

The criteria on which the diagnosis is based are (1) the signs of an active endocarditis, (2) fever, often of low grade, (3) positive blood cultures, most often revealing the streptococcus but sometimes another organism instead, and (4) embolic phenomena, that is petechiae in the skin, red cells or albumin in the urine, enlargement of the spleen, or local symptoms from lodgment of bacteria in the brain, the lungs or the extremities. The most constant observations are fever and heart murmurs. There are, however, many mild cases of subacute bacterial endocarditis which escape recognition because of negative blood cultures.

The incidence of this infection varies year after year, as do other infections. Few cases were observed by Capps from 1910 to 1920. There was an abrupt rise in the number of cases observed in 1922, which reached the peak in 1923. A decrease was observed in the following year; then an irregular number of cases was observed from 1925 to 1937. The experience at the Massachusetts General Hospital from 1910 to 1926 is comparable. From 1910 to 1921 there occurred from two to eight cases a year; in 1922 the number increased to nine, in 1923 to sixteen, in 1924 it fell to eight, in 1925 it rose to fourteen, and in 1926 the number was again down to seven cases. The epidemic in Boston occurred, therefore, in about the same years as did the wave of cases in Chicago. Eight of the eleven cases of recovery reported by Capps occurred in the period from 1920 to 1924. He has not seen a case of recovery since 1924. The patients now considered as recovered with few exceptions were up and around when first seen complaining of loss of weight and appetite, fatigue and palpitation and sweating. They were in marked contrast to the septic appearance of most of the bed patients who died.

The numerous remedies that have been employed in the treatment of cases of subacute bacterial endocarditis in which recovery has occurred is in itself a suspicious circumstance. Transfusion of the blood of donors immunized with the patient's organism has been of doubtful value. Vaccines have failed in extensive tests, and our faith cannot yet rest on any of the several chemotherapeutic products used. Sulfanilamide has been disappointing, although it is perhaps too early to estimate its value. The patients in the Capps series who recovered, as well as most of the ones who died, were given sodium cacodylate by vein, 3 grains (0.2 Gm.) a day, over a period of from six weeks to three or four months. It is impossible to say to what extent this remedy contributed to recovery, but it probably played a minor part. The most important therapeutic measure was prolonged bed rest. The patients who recovered were kept in bed often for three or four months. These products and methods rarely had any constant value in the septic cases with high fever and embolic phenomena. The only hope of a successful outcome lies in discovering the mild cases early, and in the immediate and prolonged enforcement of bed

rest. The patient in the office and dispensary who has a heart murmur and a low fever of undetermined origin may after repeated blood cultures show Streptococcus viridans; it is not in the hospital wards that mild cases will be discovered. The elective site for the invasion of Streptococcus viridans is said to be in an old rheumatic endocarditis; a patient with a rheumatic heart valve or a congenital heart lesion is peculiarly vulnerable to this infection.

ILLEGITIMACY IN THE UNITED STATES

About 4 per cent of all live births in the United States are births of children who are illegitimate, in that the births are "out of wedlock." The figure is not absolutely accurate, because states vary in the manner of keeping birth records. Several of our states do not classify illegitimate births separately. The figures of the United States Bureau of Census indicate that about 75,000 illegitimate children are born annually, of whom 35,000 are white and 40,000 Negro. The proportion of illegitimate to total births has been estimated to be 39.8 per thousand, with a rate of 20.3 per thousand for the white population and 162.4 for the colored population. Thus illegitimate births occur approximately eight times as frequently among the colored population as among the white. These rates are reflected by those states which have been denominated as public health problem No. 1. For example, the 1936 rates for illegitimate births varied from a low of 11.2 in Utah to 101.6 in South Carolina, 85.4 in Mississippi, 84.4 in Louisiana, 83.4 in Alabama and 83.1 in the District of Columbia. Here is an obvious relation to the racial distribution of the population, similar to the relation observable in the death rates in those states.

Laws relating to illegitimacy vary greatly among the different states. A study of these laws shows that they are not adapted to modern social conditions. Previous attitudes required punishment of the man responsible for the child born out of wedlock and this attitude is still reflected in most legislation. Few laws take into account the desirability of giving a child born illegitimately equal opportunity with other children in its life after birth. The seriousness of this situation is reflected currently in articles published in the *American Magazine* and in *Collier's,* which indicate that our social attitudes are still such as to penalize the child born out of wedlock far beyond any responsibility that should rest on the child itself. Furthermore, the falling birth rate, the increasing desire to obtain children for adoption, and our social attitude toward the unwed mother and the illegitimate child have established exploitation of the unwed mother and of the illegitimate child for commercial purposes. Numerous maternity homes, such as those conducted under the auspices of the National Florence Crittenton Home, the Salvation Army and some religious organizations, maintain high standards of social and medical care, and suitable cooperation with other social agencies. Many private institutions, however, are conducted for profit and have brought into this field commercialization as despicable as any of that associated in the past with the promotion of fraudulent medicines.

In times of depression illegitimacy increases. The illegitimate birth rate in the United States rose by 12 per cent from 1929 to 1934, at a time when the legitimate birth rate decreased by 11 per cent. Marriages decrease during depression periods, but the figures show that fertility may increase. In families on relief, the birth rates are much in excess of those obtaining in families with economic independence. The extent to which enforced idleness and moral let-down are associated with dependency and relief is a problem to which social investigators might well give attention.

Finally, illegitimacy yields dependency. Fifteen per cent of the total number of children in institutions and in foster homes in 1933 were of illegitimate birth. Many illegitimate children are born of mothers exceedingly young and obviously, therefore, themselves requiring care from social agencies. Girls under 18 years of age make up one fourth or more of all unmarried mothers.

The problem of illegitimacy is not essentially a health problem but one which intimately concerns the medical profession. If our nation has lagged behind in health as some critics assert, it has certainly lagged much further behind in its social attitudes and in its legislation on this problem.

HOSPITAL SCHOOLS

Children who are confined in a hospital for treatment are unable to attend school classes; therefore they present an educational problem. This is especially true of those suffering from chronic or crippling conditions. For such children the hospital school has been developed. Clele Lee Matheison[1] reports a study of 162 hospital schools in the United States and its dependencies.

Hospital schools have been known for many years. The first was founded by a physician, Dr. Knight, of New York City, with his daughter. His home served as a combined school and hospital for crippled children. This school is still in existence. The second hospital school was established in 1882 at Baldwinsville, Worcester County, Massachusetts. The founder was also a physician whose interest in this project was aroused by seeing the cripples brought to the Bellevue dispensary. This institution is also in existence today; it is independent of any state supervision of the educational work and is financed from the hospital budget by the Woman's Auxiliary.

The movement for hospital schools has grown in a haphazard manner. Many of the schools now established have little information as to what others are doing, owing to lack of material on this subject. Laws

1. Matheison, Clele Lee, in cooperation with the Office of Education, United States Department of the Interior: Hospital Schools in the United States, Bull. 17, 1938.

differ with the different states. Private initiative was responsible for promoting the idea in the first place and for later development and financial support. The Rotary International has been one of the most influential organizations in the promotion of this movement. Other organizations have followed suit and are now continuing their influence even to the extent of added financial assistance where the state has already begun to contribute toward support of the hospital school. The development of state educational responsibility has been slow. At present seventeen of the forty-eight states have laws relating specifically to hospital schools for the physically disabled child. The physically disabled adult and mentally deficient patient are not included under these provisions, since the rehabilitation laws of various states are intended to take care of these groups. The laws now in effect contain either mandatory provisions or permissive legislation for the establishment of hospital schools. Some states have both. The mandatory provisions usually provide for crippled children and are optional as far as other physically disabled children are concerned.

Conservative estimate of the number of schools in existence is between three and four hundred, a number entirely inadequate to meet the needs of the number of children requiring their services. The aims of the hospital schools are (1) therapeutic, (2) vocational and (3) to give the child the education to which he is entitled and would receive under normal conditions in the regular schools. Since the education of the physically handicapped child cannot be continuous, such children may show a greater amount of retardation than is found in the regular school. This retardation is not due to low mentality on the part of the hospital school children but is due primarily to the lack of opportunity for education during the hospital stay. There appears to be a need for further study of existing schools and for much additional help so that crippled children may have the education they need to cope fairly with a world which they enter under a disadvantage.

Current Comment

UNNECESSARY SURGERY

Much of the propaganda devoted to breaking down public confidence in the American medical profession in recent years has been devoted to an attack on the medical profession because of the performance of allegedly unnecessary surgical operations. Obviously, this kind of propaganda is never supported by facts or figures but is largely devoted to what has come to be called "a smearing campaign." In contrast is a report recently made available of surgery performed in a Brooklyn hospital. According to figures supplied by Dr. S. S. Goldwater, Commissioner of Hospitals, New York City, major surgical operations were performed in that hospital on 979 patients, exclusive of operations on bones and joints, and fractures and other lesions of bones and joints were treated to the number of 788. At the same time in this institution sixty-eight patients with possible surgical conditions were treated conservatively without operation, and 117 patients who came into the hospital with surgical diagnoses were not operated on because further study failed to confirm the diagnosis. THE JOURNAL ventures to say that this type of figures could be duplicated in the vast majority of hospitals in this country and particularly in those institutions approved by the Council on Medical Education and Hospitals of the American Medical Association as institutions suitable for the training of interns; moreover, the staffs of most hospitals maintain the same conscientious attitude toward the patients under their care.

HOMICIDE BY WITHDRAWAL OF INSULIN

A person who induces a diabetic patient to discontinue the use of insulin, when the use of that drug is necessary to preserve his life, is guilty of manslaughter if the patient dies as a result of such action. In principle, it is equivalent to withholding insulin from the diabetic patient by physical force. Intelligent public opinion everywhere will approve of the decision of the Supreme Court of Washington, abstracted elsewhere in this issue, branding as a killer a so-called drugless healer whose negligent treatment of a person with diabetes caused death. The court said that such conduct constituted manslaughter. The healer not only assured the patient that insulin was absolutely unnecessary for his recovery but induced him to discontinue a diet prescribed by a reputable physician, limiting the use of carbohydrates. A similar case was reported in the London letter in THE JOURNAL last year.[1] A young school teacher in London had been under medical treatment for diabetes for a number of years. Her condition was satisfactory and was likely to remain so as long as she followed the dietetic instructions of her physician and continued the use of insulin. On the recommendation of friends, however, she went to see an osteopath, who told her that she did not have diabetes but was suffering from anemia, and the patient was persuaded to discontinue the use of insulin and to limit her food for a period of several days to orange juice every two hours. As a result of this treatment she died and the osteopath was convicted of manslaughter and sentenced to six months in prison. In the United States, persons without scientific training and utterly ignorant of the causes, diagnosis and treatment of disease, faith healers and other incompetents are permitted either by sanction of law or by toleration to assume responsibility for the treatment of sick human beings. As long as they are permitted to do so, tragedies such as the one that occurred in Washington must and will occur all too frequently. Here is a condition that is being given scant consideration in the current proposals for promoting the health of the people. The most fundamental factor in every consideration of medical service is the scientific qualification of those who render the service.

1. Osteopath to Be Tried for Manslaughter, J. A. M. A. **110**: 2164 (June 25) 1938. Osteopath Sent to Jail, ibid. **111**: 731 (Aug. 20) 1938.

ORGANIZATION SECTION

MEDICAL FEES FOR OBSTETRIC SERVICE

R. G. LELAND, M.D.
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CHICAGO

Emoluments received from the practice of medicine do not involve the transfer of a tangible material commodity. A physician's professional relations with the public are classified by economists as personal service. They are not subject to resale; therefore they have no basic exchange value. These personal services differ in many ways from those furnished by the other professions. The attorney, in civil cases for instance, is concerned with tangible values, subject to legal action. Even in the majority of criminal cases he can bargain in advance for his fees, and he can secure himself in almost any professional transaction by a retainer fee. The architect or engineer is concerned with structures subject to a lien or other legal action. But it is not customary for the physician to pledge himself by the acceptance of a retainer fee, nor can he secure a lien on the human body.

The medical profession is concerned with the development and application of efforts to conserve human values. Economists, as well as physicians, recognize the inherent difficulties in arriving at any accurate or even approximate statistical measurement of vital values, such as health and life. Vital values, however difficult to determine, must be stated not only in terms of the person valued but also in terms of those for whom the individual has value. Such determinations must include the worth of the individual to himself, his family and his dependents, his business associates, the state and the world or society at large. Not the least among these considerations should be the part which the individual can and should perform in maintaining local, national and world population increments. It should be self evident that the values ascribed to an individual depend on his ability to function as a normal, healthy member of society.

An understanding of these vital values and the dissimilarity of individuals and their physical and mental reactions is an important part of the practice of medicine. Because of these variables, good medical care always has been and always will be an individual service involving a close, personal, confidential relationship between the patient and the physician of his choice. Thus, health requirements and the means for their maintenance or improvement cannot successfully follow the assembly line technic of industry, and the cost price principle of business and industry cannot be used by physicians in establishing fees for their services.

In the field of obstetrics the midwife appears to be one of the most ancient of professional figures. During the early periods of medicine, physicians were accustomed to leave the care of women's diseases and obstetrics to midwives, and indeed this was the practice in America until shortly after the middle of the eighteenth century, when William Shippen first removed the prejudices in opposition to male accoucheurs.

FEE SCHEDULES

When we turn to early American medicine, we find that such medical legislation as the colonies had in this period was, as in the Code Hammurabi (2250 B. C.), mainly concerned with the momentous question of fees. An example of one of these early American regulations is to be found in volume 4, Hening's Statutes at Large of Virginia, page 509, "An Act of Regulating the Fees and Accounts of the Practice of Phisic," but no mention is made in the list of allowances of any fees for obstetrics.

The account book of John Warren, dated May 1782, contains a list of charges entitled "List of Fees of the Boston Medical Society." This list contains the item "for midwifery, 2 pounds 8 shillings." In 1817 the Boston Medical Association listed charges for midwifery during the day as $12 and at night $15.

The New York City Fee Bill of 1816, which was a renewal of that of 1790, differed from the Boston Fee Bill in the greater latitude of charges and the larger number of items. Midwifery in New York was more expensive than in Boston, the charges being from $25 to $35 in common cases and from $35 to $60 in tedious or difficult cases.

Philadelphia, with medical talent unsurpassed in America, had a relatively low fee bill. In 1834 the charge for midwifery was from $8 to $20—nearly comparable to the charges in Boston but less than the fees in New York City. In 1833 the midwifery charges in Washington were $12 in the day and $15 at night. In the small towns, medical fees were much lower; e. g., in Lowell, Mass., the charge for midwifery was $5.

The Ohio legislature at its session of 1836-1837 granted a charter to "The Lebanon Medical Society." One of the first acts of this society was to adopt a fee table which included the items "common cases of parturition $5, protracted or difficult $5 to $20."

In 1871 the Omaha-Douglas County Medical Society adopted a fee schedule which lists "obstetric fees, ordinary case of not over six hours $20; for each hour's attendance over six hours $1."

Although the index numbers of prices and money values for the early decades of the United States are not accepted as having a high degree of accuracy, there seems to be little doubt that the purchasing power of money at that time was at least 100 per cent greater than it is today.

A study of the development of fee schedules for medical services during the early period of American history reveals some of the factors that physicians of those times considered, in an effort to arrive at fair

Read before the Public Health and Hospital Administrators Section of the American Congress on Obstetrics and Gynecology, Cleveland, Sept. 14, 1939.

charges for their services. It was recognized that distance, time, economic status, educational attainments and professional skill should be considered in fixing medical fees. These same factors are still important in determining charges for medical care, but, with the perfection of new methods and technics, costly drugs and procedures in diagnosis and treatment, and the growing appreciation of these new developments on the part of the public together with the increasing complexity of modern society, new factors have added to the difficulty of establishing medical fees which would permit the use of new and sometimes expensive procedures and would at the same time be fair to the patient.

Wherever fee schedules have been adopted, they have represented the considered opinion and the established custom of the physicians in small areas, usually cities or counties. Moreover, the physicians in many parts of the United States still prefer to follow common custom rather than an adopted schedule of fees.

The Bureau of Medical Economics has assembled the fee schedules reported to have been adopted by 559 county or district medical societies in forty-six states. The composite list of fees compiled from these schedules comprises 606 items. This composite list, when compared with the small number of items listed in the earliest fee bills, provides some index of the developments in medical science and practice over the past 150 years.

The items in this composite list of fees under the classification "Obstetrics" include:

Normal delivery—one child.
Normal delivery—more than one child.
Induction of labor.
Abnormal presentation or position.
Version.
Premature delivery.
Delivery by forceps.
Treatment of placenta praevia, convulsions, or other abnormalities or complications.
Treatment of abortion.
Treatment of miscarriage.
Craniotomy or embryotomy.
Ectopic pregnancy.
Delivery of placenta only.
Cesarean section.
Severe postpartum hemorrhage.

In some localities the charges for antepartum and postpartum care are in addition to the fees listed for delivery, but in other places it is impossible to judge from the fee schedules whether or not the stated fees for obstetrics include antepartum and postpartum care.

Available source material includes 491 schedules which give the charges for "normal delivery—one child." The range of minimum charges in these schedules is from $10 to $75, with a median of $25. Maximum charges for the same items are given in 105 schedules, with a range of from $15 to $1,000 and a median of $50.

The medians of minimum and maximum charges for other obstetric services are given in the accompanying table.

These median charges represent a position average. They are not influenced by the size of the fees above and below them but represent the central tendency in a series of high and low fees.

The fee bills of early American medicine and the 1938 fee schedules of county medical societies give some idea of the variation in charges for medical services in different communities. A casual comparison of the charges today and those of a century ago indicates that, in general, the value ascribed to medical services by physicians has changed but little during the century. However, when it is realized that during the early part of the nineteenth century the purchasing power of money was about 100 per cent greater than it is at present, it is clear that medical fees today are actually far below those of the early decades of the United States.

Although it can be shown that many of the basic charges for medical services have remained almost stationary over a century or more, the aggregate of medical fees has increased in the wake of a continuously accumulating fund of medical knowledge and a multiplication of the number and nature of available medical services. The new technics of diagnosis and the new methods of treatment have not only provided greater assurances of prevention or of recovery from disease but they have also introduced new procedures in medicine which are sometimes costly and which could not have been included in earlier fee schedules.

DIFFICULTY OF GUARANTEEING GOOD MEDICAL CARE FOR EVERY ONE

As the number, variety and value of medical services have increased, the public has gradually grown to demand all and sometimes more than the medical profession could provide in the care of some classifications of disease. Indeed, in the face of the most gratifying health conditions ever reached by any 130,000,000 people at any time, made possible by the methods of medical practice that have been maintained and advanced in the United States, the public has only recently been surfeited with costly publicity and propaganda. The chief object of this would appear to be to create in the public mind a growing dissatisfaction and a waning confidence in present medical services, to bring discredit on the humanity, competence and services of the health professions, and to advance a new form of medical practice.

It may be well to cite some of the conditions which make it difficult, if not impossible, to guarantee good medical care to every one. Genes and germs are still responsible for certain conditions that are beyond human control. Accidents and ignorance are still operating to deprive individuals of legs, arms, sight and other health attributes. Superstitions and personal preferences still place good medical care beyond the desire of some people. Indeed, there have been instances in which court orders have been necessary to permit the use of medical science to save the lives of children.

Predictions that definite numbers of persons can be spared the experience of illness or can be guaranteed a longer span of life are without any basis of fact. Too frequently those who make such predictions fail to consider the human factor. Blame for many individual health defects, if blame is to be attached, belongs to the individual himself. No one, however skilled in medicine, and no method, however perfect, could keep some people continuously in health.

Above all, technical minds should realize that, while expansion and improvement of the public health and curative service in the nation are long overdue, the individual has some responsibility for his health and that of his family. There is a possibility that medical science is being pressed too hard for cures of hereditary,

constitutional and neglected disease. We must not lose faith in the ability of the individual to accomplish some measure of betterment himself in social and health matters, if given the enlightened guidance of health education.

When all these and many other factors are considered, it should be evident that the mere fact of the availability of medical services gives no assurance that such services will be used by persons who need them. Moreover, it must be admitted that even the most skilled physicians cannot accomplish the impossible.

Medical ethics, which places service to humanity above the income determining elements of medical practice, has survived as the strongest stimulus to good medical service.

FORCE OF CUSTOM IN FIXING FEES

From whatever point of view the problem of charges for medical services is approached, the conclusion is always reached that the dominant force in fixing fees is custom. Every attempt to establish an hourly rate as a "value of services rendered" is complicated, if not entirely thwarted, by the introduction of such "vital values" as life and health, which defy market valuations.

Some forms of organized medical service have attempted to follow industrial models and have fixed their charges according to the "cost of production." The determination of the cost of production in medicine is possible only as far as the items priced are already standardized on industrial lines. For example, a hospital can calculate the cost of rent, interest on invested capital, depreciation of buildings and equipment, expenditures for food and other commodities, but the medical services rendered in the hospital do not seem to permit of cost analyses by any accounting or valuation technic known at present.

The custom-fixed measure of the value of medical services is far from rigid. Wide variations by individual physicians for individual patients are common; this is known as the "sliding scale" of fees, by which charges are varied according to the patient's ability to pay. Moreover, that principle of medical ethics which states that "the poverty of a patient and the mutual professional obligation of physicians should command the gratuitous services of a physician" is observed by the medical profession now, as in the past. Indeed, medical care is one of the few necessities of life still available to those who have no money, but the volume of demand for free services during recent years has become too great for physicians to bear alone.

It is not claimed that the present system of charges for medical care is perfect, but the overwhelming majority of physicians are endeavoring to render good medical services at fair fees. Unfortunately, an occasional unwarranted charge is publicized as if it represented the general rule. Moreover, it must be recognized that human nature, illness and the treatment of disease cannot be standardized, and therefore charges associated with attempts to apply the mass production principle in medicine do not always represent good values in medical care.

The salaried obstetrician in a teaching institution is an example of the exception to the general rule of fee for service. Such physicians are animated by an approach to a perfect performance made possible by the favorable conditions created and maintained by these institutions. The primary motive of teachers of obstetrics is devotion to the improvement of methods which will advance the general practice of obstetrics and enhance the benefits to mothers and their children. These conditions and motives could not be made a part of a general scheme to place all obstetricians on salary.

Obstetric practice today is immeasurably superior to the midwifery care of 150 years ago. There is every reason to expect that in the field of obstetrics, as in other special fields of medicine, new procedures and services will continue to be developed for the benefit of new generations and their mothers. These new procedures and services cannot be provided without cost to some one. The extent to which such benefits are to be considered as regular services for all normal obstetric cases or special services for the exceptional cases cannot be determined as a hard and fast rule. Neither is it possible, under a democratic system of government, to compel expectant women to consult a physician and to remain under his observation from the first sign of pregnancy, even though all mothers and children might benefit thereby.

Median Charges for Obstetric Services

	Minimum	Maximum
Normal delivery, more than one child	$ 45.00	$ 100.00
Induction of labor	50.00	500.00
Abnormal presentation or position	30.00	.....
Version	50.00	100.00
Premature delivery	32.50	150.00
Delivery by forceps	40.00	100.00
Treatment of placenta praevia, convulsions or other abnormalities or complications	50.00	125.00
Treatment of abortion	25.00	50.00
Treatment of miscarriage	25.00	50.00
Craniotomy or embryotomy	50.00	200.00
Ectopic pregnancy	150.00	1,000.00
Delivery of placenta only	15.00	50.00
Cesarean section	150.00	500.00
Severe postpartum hemorrhage	50.00	125.00

Much more progress than is often admitted has been made in obstetrics. Further progress will depend on scientific research, the development and maintenance of confidence in the independently practicing physician, and education of the public to its responsibility in the prevention and control of abnormal obstetric conditions.

No system of payment for obstetric and other medical services can be completely and successfully separated from the varying human natures that will require medical attention, or the trained men and women who must render the services. No obstacle should be erected to discourage a continued study of improved methods of distributing medical services, or the operation of the principle that, in whatever way the cost of medical services may be distributed, it should be paid for by the patient in accordance with his income status and in a manner that is mutually satisfactory.

Any discussion of medical fees suggests that serious consideration be given to the broader and more important issue of the ability of the family to provide itself with the necessities of life. Obstetric care, however ideal, complete and reasonable in cost, cannot be a substitute for the food, clothing, heat and shelter that are essential to both mother and child. Interest in the size and the method of payment of obstetric fees should not, therefore, dispel a serious concern over the family's general economic status.

GRADUATE MEDICAL EDUCATION

A PROGRESS REPORT OF THE FIELD STUDY ON GRADUATE MEDICAL EDUCATION IN THE UNITED STATES BEING CONDUCTED BY THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

OHIO

COMMITTEE ON EDUCATION OF THE OHIO STATE MEDICAL ASSOCIATION

At the 1936 annual meeting of the Ohio State Medical Association, the constitution and by-laws of the association were revised to provide for a new representative committee, known as the committee on education, composed of five physicians appointed for five year terms. The purpose was to extend the educational activities of the association for the benefit of its members and of the public. Dr. Clyde L. Cummer, Cleveland, has been chairman of this standing committee since its inception. The committee was empowered to select subcommittees, subject to the approval of the council of the association. Four such subcommittees were selected, each headed by a member of the committee on education: (1) regional postgraduate lectures, (2) speakers' bureau, (3) district meetings and (4) public health education. The first and second subcommittees have been concerned largely with graduate instruction.

Regional Postgraduate Lectures. — The subcommittee on regional postgraduate lectures is now composed of twelve members. Continuity of its membership is provided, making possible a continuous program of instruction. The subcommittee acts as a coordinating agency and in an advisory capacity to other committees of the association. The work of this subcommittee is essential in the development of the state association's graduate program.

A five year program of postgraduate education was begun in October 1937 after extensive studies had been made of similar activities of other states. Seven cities in five regions of the state were established as teaching centers, in each of which there are ample clinical facilities. This was the state association's response to the expressed need of the profession for postgraduate programs of practical value given in proximity to the homes of physicians. A series of eight fortnightly sessions of two lectures and discussions each were given the first year and a series of six sessions of lectures constitute the second year's course being given this autumn—the time of year when all sessions are now held. Identical courses were arranged for all regions once each year.

Graduate programs were arranged in sequence and provided for continued consideration of subjects in the fields of medicine, pediatrics, obstetrics and surgery and topics of special interest chosen in proportion to their relative importance in the general practice of medicine. A regional committee was selected in each locality with representatives from each county medical society. The postgraduate lecture course was organized separately from the regular meetings of councilor district societies, and the regions selected for graduate courses were not identical with district areas.

The subjects were selected by the committee on education and the subcommittee on regional postgraduate lectures according to the needs of practicing physicians. Included in the first year of instruction were arthritis, dermatology, diabetes, gynecology, heart and intestinal disease, infectious diseases including pneumonia, poliomyelitis, syphilis and tuberculosis, antepartum and postpartum care, and management of pregnancy, psychoses and urology.

Subjects chosen for the second year included appendicitis, asthma, cancer, cardiovascular disease, obstetrics and gynecology, ophthalmology, pediatrics, poliomyelitis, proctology and syphilis.

Lecturers were chosen from physicians within the state and included faculty members of the Ohio medical schools. An effort was made to select lecturers who were able to present scientific and clinical discussions in a practical manner. Their names were listed by the speakers' bureau, which completed its organization during the first year. There are now available 300 physicians.

At the end of the first year all proposed regions of the state had been covered and the total cost, including administrative expenses, was approximately $2,783. This amount included expenses of printing programs and other announcements, publicity, postage, rental of halls and traveling expenses of instructors who gave their services gratuitously. Without the wholehearted cooperation of volunteer lecturers, the program would not be possible as now organized. Sixty-six members of the association had given lectures to physicians from seventy-seven counties during the year and 1,452 physicians, chiefly of the 6,404 members of the Ohio State Medical Association, had enrolled. There are 9,117 physicians in Ohio. Names of physicians attending these lectures were published in the journal of the state medical association. By increasing the annual dues of the state medical association from $5 to $7, it has been possible to finance the graduate program without charging registration fees.

The state association's graduate program has been developed by the committee on education and its subcommittee on regional postgraduate courses with the approval of the council of the association. Details of organization and administration, stimulating physicians' interest in continuation study and other matters concerning publicity, promotion and local arrangements, have been encouraged and developed by the executive officers of the association, assisted by the local committees on arrangements.

Speakers' Bureau.—The subcommittee on the speakers' bureau, Dr. Russel G. Means, Columbus, chairman, was organized by the committee on education to provide competent speakers for the regional postgraduate lectures and to aid local societies with their programs. Physicians who were well qualified to present effectively modern points of view were invited to participate in the state association's activities.

A cross index file has been developed according to subjects and the locations of speakers. The most successful lecturers thus far have been those accustomed to public speaking, able to talk fluently and forcefully without manuscript and with only occasional reference to notes. It has been possible to obtain speakers with extensive professional experience who give in effect dry clinics, although clinical material has not as yet been utilized.

On completion of the work of this special subcommittee in 1937 and after the bureau had begun to function effectively, the committee was discontinued and the executive secretary of the association was designated as manager to conduct the routine activities of the bureau.

District and Annual Meetings.—The subcommittee on district meetings was organized following the recommendation of a special committee of the council, of which Dr. J. H. J. Upham was chairman. Since 1935 the council has made appropriations to provide annual subsidies of $200 for each district society to aid it in securing speakers and for promotional activities. The state association exercised some general supervision over the scientific phases of the district meetings. This was to insure adequate programs, suitable meeting places and proper publicity. A pamphlet has been prepared for distribution to district society officers which suggests the fundamental factors in a successful district meeting. Thus interest in district meetings has been renewed to the extent that this year the council discontinued the district subsidies, nominal registration fees now financing these meetings, and dissolved the subcommittee on district meetings, it having served its original purpose of reviving the district meeting set-up.

The annual meeting of the Ohio State Medical Association is held in one of the larger cities of the state over two days each year. Seven guest speakers and about seventy-five Ohio physicians participated in the 1939 program, at which twelve round table conferences were an innovation. Registration of physicians at the annual meeting approximates 1,500.

Public Health Education.—The subcommittee on public health education, of which Dr. Carl A. Wilzbach, Cincinnati, is chairman, continues to cooperate with official and nonofficial health

agencies in providing the public with information regarding public health and preventive medicine. Subjects are recommended by this subcommittee to the subcommittee on regional postgraduate lectures and, when desirable, subsequent talks are presented to the public.

ACADEMIES OF MEDICINE

In several sections of the state, county medical organizations have provided postgraduate courses. Some of these have been intensive, compact series of lectures given in one or two day periods once a year, while others have consisted of a series of from ten to twenty one hour lectures in general and special subjects over several days. The metropolitan areas with their ample clinical facilities supplement the state association's graduate activities for physicians practicing in the more sparsely settled areas of the state.

One of the best known programs given in metropolitan areas is the series of postgraduate lectures conducted each year by the Cleveland Academy of Medicine. In 1937 the academy's committee on postgraduate course, Dr. R. L. Haden, chairman, adopted definite principles. These were that lectures be continuous, unified as to subject, with careful selection of speakers, and that they be limited to ten talks given at weekly intervals each year. The courses were open to all physicians without registration fee. Continuity of personnel in succeeding postgraduate committees has assured that each year's program fits into a general educational plan.

The academy's postgraduate course for 1939 included lectures in treatment, vitamins and endocrine disorders. Lectures given in the auditorium of the Allen Memorial Library Building from 5 to 6 p. m. during January, February and March were attended by 498 physicians. Notices for these programs were sent to physicians in the fifth district, which includes Cuyahoga, Lake, Geauga and Ashtabula counties.

A three to five day annual postgraduate program has been held in Toledo since 1923. This is sponsored jointly by the Toledo University and the Academy of Medicine of Toledo and Lucas County. Usually a symposium on one subject constitutes the lecture program. Other one day postgraduate programs have been given by the academy since 1934 in collaboration with the university. A fund is available for graduate medical education given under the auspices of the university. No registration fees are charged.

In April 1939 the four day postgraduate course held in Toledo was devoted to lectures and clinical pathologic conferences on gastro-enteric diseases. A guest lecturer participated in the sessions, which were attended by 125 physicians. Dr. James A. H. Magoun was chairman of the postgraduate program committee.

The Columbus Academy of Medicine presented its first postgraduate day in June 1938. Three guest speakers participated in a general program of six lectures. No registration fees were charged. In 1939 two guest lecturers contributed to the program and 125 physicians attended.

The Lima and Allen County Academy of Medicine has held a postgraduate week each year since 1930. One or more guest speakers participate. The annual attendance approximates 150 physicians.

GRADUATE ACTIVITIES OF OTHER METROPOLITAN MEDICAL SOCIETIES

In Youngstown the Mahoning County Medical Society has held a postgraduate day each year since 1928. This program is designed for physicians practicing in the vicinity, but it attracts many from surrounding counties. In 1937 a series of eight weekly lectures in pathology was given. In 1938 a postgraduate day was conducted by three guest speakers. These lectures were attended by 487 physicians.

In 1939 the postgraduate day was presented by four members of a medical faculty on general subjects of medicine. A registration fee of $5 has been charged.

Beginning in 1935 the Summit County Medical Society sponsored the first of a series of four postgraduate days in Akron hospitals. This was to enable practicing physicians to study special practices and to obtain from them points of view on general medical problems. The initial meeting was attended by 180 physicians. For three years before, graduate programs had been held in a local hotel and were participated in by out of state speakers.

Postgraduate days have been held in Canton at which guest speakers participate in a series of lectures usually devoted to a general subject of medicine.

MEDICAL SCHOOL PROGRAMS

During March 1939 the Western Reserve University School of Medicine and the staff of the City Hospital of Cleveland offered practicing physicians a lecture course on recent advances in medicine, surgery and special subjects. The auditorium of the city hospital was used three days each week during midday. Periods were allowed for discussions following twenty lectures on such subjects as endocrinology, gynecology, heart disease, tuberculosis and other diseases of the chest, diseases of children, diseases of the skin, diseases of the blood, metabolism and vitamins. From thirty to forty physicians were in attendance. A similar program is to be given in October 1939. No registration fees are charged.

A course of eight lectures on various aspects of syphilis was given over a period of eight weeks during the spring of 1938 and 1939 under the auspices of Western Reserve University, the United States Public Health Service and the Ohio State Department of Health. Lectures were held in the auditorium of the library. Members of the university faculty and health officers participated in the instruction. A full time three months course in syphilis has been available at the medical school also. Physicians have had the opportunity to enroll for shorter periods by selecting one or more weeks of instruction on a part time basis. Participation in clinical exercises, laboratory diagnosis and pathologic and round table conferences were included. No registration fees were charged. Twenty-seven physicians have enrolled.

The Ohio State University College of Medicine has held annual three day graduate assemblies in Columbus since 1934 for physicians residing in central Ohio. Dr. Russel G. Means has been chairman of the faculty committee on postcollegiate instruction for the past five years. Summaries of recent contributions to medicine by members of the faculty, dry clinics, brief reports and round table discussions have been included. General and special clinics, medical rounds and clinical pathologic conferences constitute the varied program, which was participated in by four guest lecturers in 1939. Attendance has ranged from 190 to 300 physicians. A fee of $2 is charged for registration and for a copy of the proceedings of the assembly.

The University of Cincinnati College of Medicine each year has provided one week of postgraduate instruction in otolaryngology. This course is available to practicing otolaryngologists and includes anatomic studies. Classes are limited to twenty-five. A tuition fee of $60 is charged. In addition there is an annual alumni day at which guest speakers participate.

OHIO DEPARTMENT OF HEALTH

From May 1937 to February 1939 the Bureau of Child Hygiene of the Ohio Department of Health offered instruction during one afternoon and evening in fourteen counties of the state. The first courses were given in southeastern Ohio. Obstetric instruction was given in eleven centers and pediatric talks in eight. The Ohio State Medical Association and the various county medical societies assisted on details and publicity. Subjects for discussion were selected by the bureau of child hygiene. Lectures, clinics and symposiums and round table discussions were attempted in public buildings such as churches and sometimes in hospitals by instructors from within and in one case from outside the state. Clinical demonstrations were provided at two of the medical schools. Instruction has included consideration of endocrinology, vitamin deficiencies, blood dyscrasias, infant feeding, children's dentistry, infectious diseases and eclampsia, toxemias, instrument deliveries, analgesics and hemorrhages. Approximately 383 physicians registered in pediatrics and 278 in obstetrics. No registration fees were charged, since these courses were financed with social security funds. Each speaker was paid an honorarium and traveling expenses.

OTHER GRADUATE ACTIVITIES

The Frank E. Bunts Institute has offered since November 1935 three day programs at the Cleveland Clinic three times each year. These courses are open to graduates of approved medical schools. Registration fees have varied from $5 to $10. Symposiums on subjects of general or special interest have been included, such as gastro-enterology, genito-urinary disease, endocrine disorders, diseases of the skeletal and nervous, blood and cardiovascular systems, and benign and malignant tumors. Lectures, clinics, demonstrations and exhibits have been offered. One or two guest speakers may participate. From 105 to 142 physicians from six to eight states register for these programs. More comprehensive courses in ophthalmology and diseases of the ear, nose and throat have been given also.

The Cleveland Medical Library Association occupies the Allen Memorial Library Building adjoining Western Reserve University. Since 1933 membership dues have been reduced, and other sources of income and assets of the association have proved adequate. At present there are 487 members and, while any physician may use the library, only members can withdraw reference material. Membership dues are $10, junior and nonresident membership being $5. There were 53,681 volumes and 444 files of periodicals available in 1938. During that year 12,828 visits were made to the library, the majority by nonmembers.

OFFICIAL NOTES

COUNCIL ON INDUSTRIAL HEALTH

The fourth meeting of the Council on Industrial Health took place July 8 at the Association headquarters. Those attending were Stanley J. Seeger, chairman, Harvey Bartle, Leverett D. Bristol, Warren F. Draper, Leroy U. Gardner, Henry H. Kessler, Anthony J. Lanza, Robert T. Legge, C. W. Roberts, Clarence D. Selby, Roscoe L. Sensenich (ex officio), Olin West (ex officio) and Carl M. Peterson, secretary. Transactions of interest to the profession were as follows:

1. The Committee on Rules presented for discussion precepts which should guide the Council in its relations with other professional and nonprofessional agencies interested in improved standards and conditions relating to industrial health. A list of these agencies was ordered to be prepared.

2. The Committee on Nomenclature reported progress in its compilation of terms used in industrial health and related fields. It is expected that a complete draft will be available before the end of the year.

3. The Committee on State Associations reported that the Council is in regular correspondence with thirty committees on industrial health or related groups in the state medical associations. It was recommended that continued effort be made to complete the roster of committees in the state medical organizations and to suggest to those already in existence that, as activities expand and membership increases, the highest caliber of personnel be sought after.

In the conviction that some effective means of interchange of ideas and information by the Council and the state committees would enhance organization, provide a measure of uniformity of action and stimulate wider initiative, the Council agreed to continue publication of an industrial health bulletin to be mailed from time to time to state committees and other interested groups. Through this bulletin it is expected that objectives may be more rapidly realized.

It was also decided that effort should be made to urge the attendance of members of state committees and officers of state associations at the next Annual Congress on Industrial Health, at which time a round table discussion dealing with urgently pressing problems would be undertaken.

4. The Committee on Education and Publications reported that it is continuing to gather information about undergraduate, graduate and postgraduate education in the theory, organization and practice of industrial health.

The necessity for formulating a publication program through the medium of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION was emphasized, in order to keep the profession apprised of the Council's activities and to meet the need for special information on industrial health subjects.

A canvass of state medical societies revealed almost complete neglect of industrial health as a subject for continuation studies under the auspices of committees on postgraduate medical education. It was realized that the objectives of the Council would be enhanced if a definite program of postgraduate study could be formulated. The Council resolved, therefore, to prepare a syllabus on postgraduate education and that as soon as an acceptable one had been developed the committees on industrial health in the state medical associations would be notified. It was also ordered that the Council on Medical Education and Hospitals be notified of these activities in order that its advice and assistance may be secured and in order that that Council may submit recommendations directly to committees on postgraduate medical education in the state associations.

The committee further reported that authoritative papers on pneumoconiosis, syphilis in industry and medical organization in industry are in the process of preparation, shortly to be available for publication.

5. An extended discussion on industrial health and its place in social security legislation occurred, following which the Council passed a resolution to be referred to the Board of Trustees which expressed the conviction that industrial hygiene affairs should continue to reside in the bureaus of industrial hygiene in the federal and state health departments but that recognition should be given to the desirability for cooperation with as well as assistance from other established agencies interested in this field having facilities for enforcement and regulation.

6. The relations between the Council on Industrial Health and the Section on Preventive and Industrial Medicine and Public Health were discussed. No action was taken pending receipt of information on an investigation to be conducted by a committee of the section designed to improve interest on the part of the medical profession in the activities of this section.

7. A committee was authorized to formulate a set of principles expressing concisely the relations which physicians should establish in industry with employees, employers and one another.

8. The Council discussed the Wisconsin Physical Examination Program as adopted by the industrial commission in that state. It was agreed that plans for industrial physical examinations in the states ought not to mature without consultation with official representatives of organized medicine. Extension of occupational disease compensation legislation will probably increase the demand for physical examination facilities, particularly in the smaller factories. The special requirements of these concerns can readily be supplied by the practicing profession if suitable information is provided. It was therefore thought desirable to investigate the possibilities for field activities in conjunction with state and county medical societies in anticipation of increased demands for industrial physical examination.

9. Reference was made to the superior methods used in Great Britain for reporting and recording the incidence of occupational disease in contradistinction to the futility of attempting to obtain comparable reports on such matters in the individual states at present. Although no specific action was taken, further information is being requested at the present time from such organizations as may be presumed to have considered these matters.

10. The Council undertook to hold its second Annual Congress on Industrial Health Jan. 15 and 16, 1940, in Chicago. It was recommended that symposiums on syphilis in industry, physical examinations in industry, disability evaluation and rehabilitation be arranged.

11. A special Industrial Health issue of THE JOURNAL having been authorized, responsibility for the Council's contributions was assigned to the Committee on Education and Publications.

12. A resolution was adopted petitioning the Board of Trustees for further assistance in the development of educational exhibits on industrial health to be available to the profession through the state medical societies.

WOMAN'S AUXILIARY

THE 1939-1940 HYGEIA CONTEST

The American Medical Association offers $300 in cash prizes to the county and state auxiliaries obtaining the largest number of subscription credits to *Hygeia* during the months of October, November, December and January. The $300 will be divided into the following cash prizes:

County Auxiliary Prizes

The county auxiliary societies will be equally divided into four groups of 100 societies each, the first group with a membership of from one to thirteen; second, from fourteen to twenty-three; third, from twenty-four to forty-two, and, fourth, those with a membership of forty-three or more.

Three cash prizes will be given to each group: first prize, $35, second prize, $20, and third prize, $10.

State Auxiliary Prizes

Two cash prizes will be given to state auxiliaries that have the highest rating based on their paid auxiliary membership and *Hygeia* credits obtained: first prize $25, second prize $15.

Last year the contest covered only the months of December and January. The three cash prizes of $50 each were won by Union County, Ark., Berks County, Pa., and Cook County, Ill. This year the time has been increased to four months and the cash prizes to $300.

For years the Woman's Auxiliary of the American Medical Association has recognized as one of its chief activities the promotion of the distribution of *Hygeia* through schools, parent-teacher organizations, boards of education, industrial plants, welfare workers, study clubs and similar bodies interested in education.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Norman Baker Surrenders to U. S. Marshal.—Norman Baker, who moved his "cancer cure" business to Arkansas after being accused of quackery in Iowa, surrendered to the United States marshal on a federal indictment charging him with using the mails to defraud, according to the Chicago *Tribune* September 23. Baker was freed on a $10,000 bond after his surrender. Five members of his staff who were indicted with him also gave up and were released on bonds of $1,000 each. The indictments charge that the mails were used fraudulently in connection with a plan to obtain money for a cancer cure, it was stated. Baker is proprietor of the Baker Hospital at Eureka Springs. According to the report, members of the staff who surrendered with Baker are R. A. Bellows, hospital superintendent; Dr. Orville L. Beatty, Dr. William S. Hutto, Dr. Johnson L. Statler, and H. L. Fisher. For a number of years Baker ran a "sanatorium," radio station and a magazine and newspaper in Muscatine, Iowa. In June 1938 when his station had been closed following an injunction forbidding him to practice medicine without a license in Iowa he moved to Eureka Springs. In August 1937 he served a day in the Muscatine county jail and paid a $1,000 fine on a charge of practicing medicine without a license. The federal radio commission closed Baker's KTNT station in the middle of a program, it was stated.

CALIFORNIA

Lectures on Pediatrics.—The Southwestern Pediatric Society sponsored its annual course of lectures and clinical discussions at Children's Hospital, Los Angeles, September 14-15. Dr. Joseph Brennemann, Chicago, was the lecturer. The subjects of his clinical discussions were "Pulmonary Conditions in Children," "Acute Abdominal Conditions in Children" and "The Subnormal Child and His Parents," according to the announcement.

New Public Relations Counsel.—Mr. Ross Marshall has been appointed press relations counsel to the California Medical Association and the following have been named to the committee on public health education: Drs. Frank R. Makinson, Oakland, chairman; Karl L. Schaupp, San Francisco, secretary; Samuel Ayres Jr., Los Angeles; Thomas A. Card, Riverside; Lowell S. Goin, Los Angeles; Junius B. Harris, Sacramento; Dewey R. Powell, Stockton, and Charles A. Dukes, Oakland, ex officio. The creation of this committee and its work was financed by a special assessment on members of the association authorized at the 1939 annual session.

New Psychiatric Service.—A separate psychiatric department was organized at the Mount Zion Hospital, San Francisco, by reorganizing the department of neuropsychiatry into two independent services—the neurologic service and the psychiatric service. Dr. Jacob Kasanin, director of the psychiatric department, Michael Reese Hospital, Chicago, and assistant professor of psychiatry, Rush Medical College, has been appointed chief of the service. Associated with him will be Dr. Mervyn Hirschfeld, assistant clinical professor of neurology, University of California Medical School. Dr. Joseph C. Solomon, formerly on the staff of the Baltimore Child Guidance Clinic, will direct the work in child psychiatry.

COLORADO

Personal.—Dr. Thomas D. Menser, La Junta, acting head of the Otero County health department, has been appointed director of the new city-county public health unit in El Paso County with headquarters in Colorado Springs.

Officers of State Medical Board.—At a recent meeting of the state board of medical examiners Dr. John Baron Farley, Pueblo, was elected president; Rodney Wren, D.O., Pueblo, vice president, and Dr. Harvey W. Snyder, Denver, reelected secretary.

CONNECTICUT

Hospital Association Joins State Medical Journal.—In January 1940 the journal of the state medical society will appear also as the official organ of the Connecticut Hospital Association. Mr. Sidney Davidson, administrator of Grace Hospital, New Haven, will represent the hospital association on the editorial board.

Commission to Study Physical and Mental Disabilities.—The governor has appointed a commission on the treatment and care of people of the state afflicted with physical or mental disabilities. Its members are Kenneth Wynne, Esq., New Haven, judge of the superior court; John A. Markham, Esq., Hartford, attorney; Dr. William H. Coon, Easton, the only physician member of the 1939 general assembly, which authorized the formation of the commission; Dr. Wilmar M. Allen, Hartford, superintendent of the Hartford Hospital, and Dr. Creighton Barker, New Haven, secretary of the state medical society. All problems, including expenditures, incident to the care of persons with mental or physical disabilities will be studied by the commission. According to the state medical journal, at the governor's request the commission will first concern itself with a study of the conditions and administration of the Norwich State Hospital for the Insane.

GEORGIA

Industrial Meeting.—The second annual meeting of the Georgia Industrial Surgeons Association will be held at The Cloister, Sea Island Beach, October 7. Included among the speakers will be Dr. Henry H. Kessler, Newark, N. J., on "Cineplastic Amputation."

Personal.—Dr. Malcolm M. Cook, Minneapolis, has been appointed director of laboratories at the Macon Hospital, effective September 1, succeeding the late Dr. Isadore J. Pass.—— Dr. Clair A. Henderson, Dawson, has resigned as health officer of Terrell County to become assistant health commissioner of Savannah.

New Building for Academy of Medicine.—Plans are under way to construct a new home for the Academy of Medicine, Atlanta. It was voted to sell the present site of the society's home, 38 Prescott Street, N.E., to Dr. Luther C. Fischer for $17,500. The society passed a motion unanimously requesting the directors of the Atlanta Academy of Medicine and Dentistry to liquidate the property and cancel the charter. The Medical Association of Georgia has moved its office from the academy to 105 Forrest Avenue.

Society News.—Dr. Jesse H. Campbell, Commerce, addressed the Jackson-Barrow County Medical Society, Jefferson, recently on diseases of the nose and throat.——Dr. Henry A. Seaman, Waycross, read a paper on "Treatment of Malig-

nancies of the Breast" before the Ware County Medical Society, Waycross, August 2.——The Fulton County Medical Society, Atlanta, was addressed September 21 by Dr. David Henry Poer on "Clinical Experiences with Use of Dihydrotachysterol (A. T. 10) in the Treatment of Ten Cases of Hypoparathyroidism." A symposium on malaria was presented before the society, Atlanta, September 7 by Drs. Charles Daniel Bowdoin, George M. Murray, Atlanta, and John W. Oden, Milledgeville.

ILLINOIS

Thirty-Five Deaths from Typhoid at State Hospital.—Thirty-five deaths have been reported in the outbreak of typhoid at the state hospital for the insane near Manteno, newspapers reported September 21. The epidemic has virtually halted for a second time construction of new buildings costing $1,500,000 at the institution, it was stated.

Society News. — Dr. Archibald L. Hoyne, Chicago, discussed scarlet fever before the Kankakee County Medical Society September 14.——The Bureau County Medical Society was addressed in Princeton September 12 by Dr. Roger T. Vaughan, Chicago, on "Differential Diagnosis and Treatment of Acute Abdominal Lesions."——At a meeting of the Greene County Medical Society in Carrollton September 8 Drs. James E. Graham and William J. Morginson, Springfield, spoke on "The Orthopedic Aspects of the Foot" and "Fungus Infections of the Foot" respectively.

Chicago

Special Joint Meetings.—Dr. Soma Weiss, Hersey professor of the theory and practice of physic, Harvard Medical School, Boston, will lecture at a joint meeting of the Institute of Medicine of Chicago and the Chicago Society of Internal Medicine October 27 at the Palmer House. His subject will be "Syncope, Collapse and Shock—Mechanism and Treatment." Dr. Harry Gideon Wells, professor and chairman of the department of pathology, University of Chicago, will deliver the fourth Christian Fenger lecture of the institute and the Chicago Pathological Society on "A Neglected Subject, Adipose Tissue" at the Palmer House November 13.

INDIANA

Personal. — Dr. Harry E. Klepinger, Lafayette, has been appointed health commissioner of Tippecanoe County, succeeding the late Dr. Frank M. Biddle, Battle Ground. —— Drs. Robert C. Speas and Edith M. B. Schuman have been named physicians for the student health service at Indiana University, Bloomington.——Mr. Paul R. Waddell has recently been appointed executive secretary of the St. Joseph County Medical Society. Mr. Waddell has worked as copywriter and account executive with advertising agencies in New York, Boston, Chicago and Pittsburgh, according to the state medical journal.

Pediatric Conference. — A postgraduate conference on pediatrics, sponsored by the Vanderburgh County Medical Society, was held in the Deaconess Hospital, Evansville, September 18. Among the speakers were Drs. Walter Russell Springstun on "Early Recognition of Rheumatic Fever"; Harold D. Lynch, "Common Feeding Problems of Infants and Children"; Dallas Fickas, "Early Recognition of Osteomyelitis"; Bernard D. Ravdin, "Diagnosis and Treatment of Acute Otitis Media in Children," and Charles F. Leich, "The Cross Eyed Child." Dr. Albert Graeme Mitchell, Cincinnati, addressed the banquet session on "Consequences of Diarrhea and What Can Be Done About Them."

IOWA

Society News.—At a meeting of the Des Moines Academy of Medicine and Polk County Medical Society September 26 the speakers were Drs. Walter D. Abbott on low back pain and Lee Forrest Hill, pleurodynia. —— Dr. Temple S. Fay, Philadelphia, addressed the Linn County Medical Society, Cedar Rapids, September 29, on "Physical and Neurological Considerations of Interest to the General Practitioners." ——Dr. Christian B. Luginbuhl, Des Moines, addressed the Hardin County Medical Society in Eldora recently on "Endocrine Therapy in General Practice."

Falls in the Home Outnumber Motor Accidents.—Falls in the home caused the deaths of more persons in Iowa during the first eleven months of 1938 than did motor vehicle accidents, according to the state department of health. For this period 462 deaths from falls were reported, as compared with 416 motor vehicle deaths. The greatest toll of lives claimed by injuries from falls was in the age group of 65 years and older. In this group 405 deaths were recorded while motor vehicle accidents accounted for 106 deaths in this group and 188 deaths of persons between the ages of 25 and 64. Between 25 and 64 forty-two deaths from falls were reported; there were ten deaths of children under 5 years, three in the age group of 5 to 14 years and two between 15 and 24 years. Polished floors, icy porches and front steps, loose rugs and toys on the floor were given as causes of falls. Several children died from injuries sustained when they fell out of high chairs. Falling out of chairs, out of bed and tripping were among the causes of death of persons in the oldest age group. The most unusual death was that of a woman who walked out of the house in her sleep and fell into a well. She was rescued but died of injuries from the fall.

KENTUCKY

State Medical Election.—Dr. Austin Bell, Hopkinsville, was chosen president-elect of the Kentucky State Medical Association at the annual meeting in Bowling Green September 14, and Dr. John W. Scott, Lexington, was installed as president. Vice presidents elected were Drs. Arthur Clayton McCarty, Louisville; George H. Gregory, Versailles, and Eldon W. Stone, Bowling Green. The 1940 meeting will be in Lexington.

Changes in Health Officers.—Dr. George F. Brockman III, Louisville, has been appointed to succeed Dr. Neale M. Atkins as health officer of Muhlenberg County.——Dr. Price Sewell Jr., formerly of Jackson, has been appointed director of a new health unit in Owen County. —— Dr. Gradie Rowntree, who has served as acting director of health of Louisville in the absence of Dr. Hugh R. Leavell during the past year, has now been appointed assistant to Dr. Leavell. Dr. James Robert Hendon will succeed Dr. Rowntree as director of activities in venereal disease control; Dr. Hendon has been acting director of this division.

MINNESOTA

University Medical School Observes Fiftieth Anniversary.—The University of Minnesota Medical School, Minneapolis, will celebrate its fiftieth anniversary October 12-14. The theme will be "Trends in Medical Progress with Particular Reference to Chemistry in Medicine." The program will include clinics, round table discussions and the following papers:

Herbert Freundlich, Ph.D., The Colloid Chemistry of Membranes in Living Organisms.
Dr. Maurice B. Visscher, The Performance of Osmotic Work in Living Systems.
Dr. John P. Peters, New Haven, Conn., Some Reactions by Which Solutes May Be Differentially Concentrated by the Kidney.
Lee I. Smith, Ph.D., Organic Chemistry in the Pursuit of Vitamin Research.
George O. Burr, Ph.D., Investigations of Metabolism of the Fatty Acids.
Dr. Charles H. Best, Toronto, Canada, Investigations Concerning the Problem of Thrombosis.
Gov. Harold E. Stassen, Medicine and the Commonwealth.
Guy Stanton Ford, Ph.D., president, University of Minnesota, The Place of Medicine in a University.
Dr. A. J. Kluyver, professor of microbiology, Delft, Holland, Microbic Respiration.
Dr. Robert G. Green, The Biology of Animal Virus Diseases.
Dr. Perrin H. Long, Baltimore, Observations on the Mode of Action of Sulfanilamide and Its Derivatives.
Dr. Henry F. Helmholz, Rochester, Minn., Chemistry in Urinary Antisepsis.
Dr. Irvine McQuarrie, The Chemical Approach to the Problem of Convulsive Mechanisms.
Dr. Herbert S. Gasser, New York, Methods of Analysis of Nervous Action.
Detlev W. Bronk, Ph.D., Philadelphia, Nervous System in the Regulation of Visceral Processes.
Dr. Harold S. Diehl, The Medical School of the University of Minnesota in Retrospect and Prospect.
Dr. Donald C. Balfour, Rochester, Graduate Medical Education.
Richard E. Scammon, LL.D., Progress in Medical Education on the American Scene.

Special lectures will include the university convocation address Thursday morning with Dr. Thomas Parran, Surgeon General, U. S. Public Health Service, Washington, D. C., as the speaker on "Medical Education, Research and the Public Health"; the first Elias Potter Lyon Lecture with Dr. Anton J. Carlson, Chicago, as the speaker on "The Role of the Fundamental Sciences in Medical Progress"; annual lecture of the Minnesota Pathological Society, Dr. George H. Whipple, Rochester, N. Y., "Production, Utilization and Significance of Blood Proteins"; the annual Alpha Omega Alpha lecture, Dr. Walter B. Cannon, Boston, "The Argument for Chemical Mediation of Nerve Impulses," and the Herman M. Johnson Lecture of the Minnesota State Medical Association, Dr. Olaf J. Hagen, Moorhead, class of 1906, on "The Medical School

from the Point of View of the Alumni." Dr. George A. Earl, St. Paul, president, state medical association, will present the distinguished service award of the state association posthumously to Dr. William J. Mayo, Dr. Charles H. Mayo, Rochester, and Dr. Herman M. Johnson, Dawson.

NEBRASKA

New Dean Appointed at Creighton. — Dr. Charles M. Wilhelmj, professor of physiology at Creighton University School of Medicine, Omaha, has been appointed full time dean to succeed Dr. Bryan M. Riley. Dr. Riley has served part time for the past six years but does not wish to devote full time, according to a newspaper announcement. He will remain on the faculty. Dr. Wilhelmj graduated from the St. Louis University School of Medicine, St. Louis, in 1922 and took the degree of master of science in 1923. After an internship he served as instructor in bacteriology and immunology at his alma mater and later on the staff of the Mayo Foundation, Rochester, Minn. The school is completing a two story addition, which will be used for the department of anatomy, additional examining rooms and laboratories.

NEW YORK

Graduate Lectures in Rochester.—The council committee on public health and education of the Medical Society of the State of New York has arranged a series of lectures for the Medical Society of the County of Monroe to be given in Rochester during October. The lectures are as follows:

Dr. John D. Lyttle, New York, Nephritis, October 2.
Dr. Ferdinand J. Schoeneck, Syracuse, New Factors Which Tend to Reduce Maternal Mortality, October 9.
Dr. John F. Erdmann, New York, Gallbladder Disease, October 16.
Dr. John J. Morton Jr., Rochester, subject not announced, October 23.
Dr. Kenneth R. McAlpin, New York, A General Consideration of Anemia, Both Primary and Secondary, October 30.

District Meetings. — The annual meeting of the Fourth District Branch of the Medical Society of the State of New York was held in Ogdensburg September 19-20. Dr. John R. Schermerhorn, Schenectady, conducted a skin clinic and other speakers were Drs. Newell W. Philpott, Montreal, Canada, on "Breech Delivery"; Arthur R. Elvidge, Montreal, "Head Injuries"; Marvin Israel, Buffalo, "Physician's Responsibility in Child Behavior Problems," and Grant C. Madill, Ogdensburg, "Carcinoma of the Colon." At an evening session Dr. Terry M. Townsend, New York, president of the state society, made an address and Dr. Emerson Crosby Kelly, Albany, described "Greek Health Resorts in 500 B. C."——The Sixth District Branch met in Binghamton September 21 with the following speakers: Drs. Marjorie F. Murray, Cooperstown, on "Analysis of Abnormalities Disclosed by Routine School Health Examinations"; Carl Eggers, New York, "Carcinoma of the Gastrointestinal Tract," and Edward C. Reifenstein, Syracuse, "Digitalis: Its Use and Abuse."

New York City

Society News.—Dr. Meyer A. Rabinowitz will give the first of the fall series of Friday afternoon lectures of the Medical Society of the County of Kings, Brooklyn, October 6 on "Abdominal Diagnosis."——Dr. Edwin B. Bilchick addressed the Bronx Otolaryngological Society September 26 on "Affections of the Sphenoid Sinus."

OHIO

Society News. — Dr. Harold M. Crumley, Chillicothe, addressed the Highland County Medical Society, Hillsboro, August 4, on "Preparation and Postoperative Care of Surgical Patients."—— Dr. Jerome Hartman, Dayton, addressed the Greene County Medical Society, Xenia, August 3 on "Diagnosis and Management of Disorders of the Feet."——Dr. Robert A. Moore, St. Louis, addressed the Richland County Medical Society, Mansfield, July 28 on "Clinical Use of Vitamin K and Treatment of Hemorrhagic Tendency in Jaundice."

Promotions at Western Reserve.—The following promotions in the faculty of Western Reserve University School of Medicine, Cleveland, have been announced, among others:

Dr. Joseph M. Hayman Jr., to be professor of clinical medicine and therapeutics.
Dr. Argyl J. Beams, associate clinical professor of medicine.
William C. Barrett Jr., Ph.D., assistant professor of histology and embryology.
Dr. William B. Wartman, assistant professor of pathology and pathologist at University Hospitals.
Dr. Joseph L. Fetterman, assistant professor of nervous diseases.
Dr. Otto L. Goehle, assistant clinical professor of pediatrics.
Dr. Walter Heymann, assistant clinical professor of pediatrics.

Second Year of Lectures.—The Ohio State Medical Association began the second year of its five year series of postgraduate lectures with a session in Mansfield September 20 for one of the five regions into which the state has been divided. Lectures in the other regions began September 28. There are six sessions in each region, two lectures to each session. Subjects for this year's study are:

Bleeding from the Uterus.
What Shall We Do for the Pregnant Woman with Syphilis?
Obstetrics in the Home.
Acute Surgical Conditions in Childhood.
Convulsions in Childhood.
The Deformities of Poliomyelitis Must Be Prevented.
The Importance of Routine Rectal Examinations.
Helping the Public Reduce the Mortality of Acute Appendicitis.
Protecting the Heart of the Patient with High Blood Pressure.
How to Handle the Patient with Asthma.
Hints to the General Practitioner in the Handling of Acute Eye Conditions.
Present Day Viewpoints on the Diagnosis and Treatment of Cancer.

OKLAHOMA

County Society to Establish Clinic for Indigent.—The commissioners of Tulsa County voted August 14 to establish the Tulsa County Medical Clinic sponsored by the Tulsa County Medical Society to care for the county's indigent. Members of the society will staff the clinic, donating their services, and the county will furnish drugs. The county physician will serve as director; the position of county surgeon will be abolished and the head of the surgical department will serve without pay. The county will give the society $300 a month for overhead expenses, including the salary of a case worker. Borderline patients must pay for their own medicines and hospitalization. Mr. Waite Phillips, Tulsa business man, agreed to contribute $6,000 for equipment of the clinic, for which the Community Fund will contribute free rent and utilities in its building.

PENNSYLVANIA

District Meetings. — The annual meeting of the Third Councilor District of the Medical Society of the State of Pennsylvania was held at Skytop Lodge in the Pocono Mountains, Monroe County, September 7. Drs. David W. Thomas, Lock Haven, president of the state society, and Walter F. Donaldson, Pittsburgh, secretary, made addresses on "Medicine Faces Crisis" and "The National Scene" respectively. Dr. Edward L. Bortz, Philadelphia, chairman of the state society commission for the study of pneumonia control, spoke on modern treatment of pneumonia. Dr. Thomas and Dr. Bortz addressed the Second Councilor District Meeting at Swarthmore September 14, and other speakers were Drs. Belford C. Blaine, Pottsville, on "Diabetes Mortality in Pennsylvania"; Chauncey L. Palmer, Pittsburgh, "Public Assistance Medical Service in Review—Insurance Medical Service in Prospect," and Thomas Grier Miller, Philadelphia, "Observations on Small Intestinal Intubation."

Philadelphia

University News.—Dr. Franklin R. Miller, assistant professor of medicine, Western Reserve University School of Medicine, Cleveland, has been appointed assistant professor of medicine and assistant director of the department of hematology at Jefferson Medical College. Dr. Miller graduated from Harvard Medical School, Boston, in 1927.

Pittsburgh

Personal.—Dr. George L. Wessels, assistant superintendent of the Allegheny General Hospital, has been made acting superintendent since the death of Dr. G. Walter Zulauf.

Society News. — Speakers before the Allegheny County Medical Society, September 19, were Drs. William C. Hutchison, McKeesport, on "Tuberculin Testing of Students"; Morris A. Hershenson, "Cardiospasm"; Harry L. Baer and Harold R. Vogel, "Biophotometric Study of Vitamin A Deficiency in 250 Dermatologic Cases."

SOUTH DAKOTA

Health Officers to Meet. — The South Dakota Health Officers' Association will hold its annual meeting in Huron October 3. Dr. William F. Mengert, Iowa City, will be among the speakers, discussing maternal and child welfare. Others include Drs. Gerald J. Van Heuvelen, Pierre, state epidemiologist, on procedure in handling contagious disease, and Joseph C. Ohlmacher, Vermillion, on the state laboratory arrangements for making tests for syphilis under a recently enacted law.

UTAH

Community Hospital Dedicated at Provo. — The Utah Valley Hospital, a sixty bed institution built with the aid of the Commonwealth Fund as a part of its program for development of rural hospitals, was dedicated in Provo September 10. Patients were admitted September 18. The new hospital serves Utah County and parts of adjacent counties within a radius of 35 miles. The plant consists of the hospital proper and the nurses' residence, which will accommodate about twenty-five nurses. It represents an investment of more than $300,000, of which about $101,500 was contributed by the community and the remainder was a grant from the Commonwealth Fund. This is the Fund's tenth rural hospital. Dr. Fred R. Taylor, Provo, is chairman of the medical staff, to which all graduate and licensed physicians with established practices in the area are eligible. At the dedication exercises the speakers included Mayor Mark Anderson, of Provo; Mr. Clayton Jenkins, secretary and treasurer of the hospital; Dr. Melville H. Manson, New York, representing the Commonwealth Fund, and Heber J. Grant, Salt Lake City, president of the Latter Day Saints Church.

WISCONSIN

Lectures on Endocrinology at Milwaukee.—The Medical Society of Milwaukee County announces a postgraduate course in endocrinology, with the following speakers:

Dr. Samuel Soskin, Chicago, Pituitary: The Master Gland, October 31.
Dr. Jean Paul Pratt, Detroit, Female Endocrinology, November 7.
Dr. Allan T. Kenyon, Chicago, Male Endocrinology, November 14.
Dr. Edwin J. Kepler, Rochester, Minn., The Adrenal Gland, November 21.

District Meeting.—The Ninth Councilor District Medical Society held a meeting in Marshfield August 31. Guest speakers were Drs. Edward L. Tuohy and Peter S. Rudie, Duluth, Minn., on "Geriatrics in Its Relation to an Adequate Energy-Producing and Protective Diet" and "Postoperative Drainage in Appendicitis" respectively. Dr. Tuohy conducted a clinical pathologic conference in the afternoon assisted by Drs. George L. Berdez and John R. McNutt, Duluth.

GENERAL

Fellowships in Psychiatry Available.—A limited number of fellowships, provided by the Commonwealth Fund and other sources of training in extramural, especially child, psychiatry are available through the National Committee for Mental Hygiene. The committee will assign fellows for one or two years to selected child guidance clinics, the term and plan for each to be determined by his needs. Candidates should have had at least two years of psychiatry in an approved mental hospital in addition to qualities fitting them for extramural service. Questions and applications should be addressed to Dr. George S. Stevenson, National Committee for Mental Hygiene, Room 822, 50 West Fiftieth Street, New York.

Southern Tuberculosis Meeting.—The annual Southern Tuberculosis Conference will be held in Charleston, S. C., October 4-6 under the presidency of Dr. William Atmar Smith, Charleston. Medical and nonmedical sections will hold meetings Wednesday and Thursday and there will be two general sessions. Among the speakers at the general sessions will be:

Dr. William B. Porter, Richmond, Va., Tuberculosis in the Medical Curricula.
Dr. Lewis J. Moorman, Oklahoma City, Tuberculosis in Nursing Curricula.
Dr. Horton Casparis, Nashville, Tenn., Present Status of Tuberculin.
Dr. C. Howard Marcy, Pittsburgh, Report of the National Tuberculosis Association Committee on Tuberculosis Among Negroes.

At the conference banquet Wednesday evening the speakers will include Drs. Kendall Emerson, New York, managing director, National Tuberculosis Association, and Harry S. Mustard, professor of preventive medicine, New York University College of Medicine, New York.

Southern Psychiatrists to Meet.—The annual meeting of the Southern Psychiatric Association will be held in Louisville, Ky., at the Brown Hotel October 9-10 under the presidency of Dr. Charles S. Holbrook, New Orleans. Among the speakers will be:

Dr. John W. Scott, Lexington, Ky., An Internist's Reaction to the Psychoneuroses.
Dr. Oscar O. Miller, Louisville, Psychiatric Medicine.
Dr. Arthur H. Ruggles, Providence, R. I., Recent Advances in Psychiatry.
Dr. Lydia G. Giberson, New York, Psychiatry and Insurance.
Dr. Emerson A. North, Cincinnati, Psychopathic Personalities.
Dr. Leon J. Saul, Chicago, Urticarial Manifestations Observed in the Neuroses.
Dr. Thomas Douglas Noble and Frederick G. Germuth, Sc.D., Towson, Md., Barbiturates, Physiologic Reactions.
Dr. Harry Stack Sullivan, New York, Psychiatrists and National Defense.
Dr. George S. Sprague, White Plains, N. Y., Some Implications of the Psychotic State.

Where Infant Mortality Has Declined.—A study of the principal causes of death in infants under 1 year old during the period 1917 to 1937 was recently published by the Metropolitan Life Insurance Company in the *Statistical Bulletin*. Diarrhea and enteritis was the leading cause of infant deaths in 1917, with a toll of 20 deaths per thousand live births, or 21 per cent of all deaths under 1 year. In 1937 only 4.1 deaths per thousand live births were from this cause. The mortality rate from premature birth was 19.1 in 1917, reached a peak of 20.2 in 1918 and by 1937 had fallen to 15.4, still outranking any other cause of death in infancy. Congenital debility was at a high point of 9.2 deaths per thousand live births in 1918 and dropped to 3.5 in 1937. Congenital malformation has been only slightly influenced by antepartum care, a chart showed. Injury at birth, which rose sharply between 1918 and 1931, has now declined noticeably, the study showed. Of the respiratory infections, bronchitis and bronchopneumonia have declined most rapidly; the peak rate of 11.1 per thousand live births in 1918 had declined to 5.6. Influenza and pneumonia have shown some improvement since 1931. Tuberculosis and diphtheria have shown notable declines, mortality from both being at one fifth of the 1917 levels.

National Safety Congress.—The twenty-eighth annual session of the National Safety Congress will be held at Atlantic City October 16-20. There will be many addresses of medical interest. One session will be devoted to "Occupational Disease Control" with the following participants: Roy S. Bonsib, chief safety inspector, Standard Oil Company of New Jersey, New York; Warren A. Cook, Zurich General Accident and Liability Insurance Company, Chicago; Dr. Arthur G. Cranch, Union Carbide and Carbon Corporation, New York; Philip Drinker, C.E., professor of industrial hygiene, Harvard School of Public Health, Boston; Dr. Leonard Greenburg, New York State Department of Labor, New York, and Willis G. Hazard, Owens-Illinois Glass Company, Toledo, Ohio. Among individual papers will be:

Dr. Albert E. Russell, U. S. Public Health Service, Chicago, Syphilis Control and Its Relation to the Food Industry.
Dr. Oscar A. Sander, Milwaukee, Metal Fume Poisoning.
Drs. Joseph V. Klauder, Philadelphia, and Elmer R. Gross, Wilmington, Del., Dermatitis Control—Proper and Improper Use of Cleansing Agents; Soap and Other Detergents.
Dr. Louis H. Frechtling, Hamilton, Ohio, Industrial Hernia and Its Control.
Dr. James W. Long, Port Arthur, Texas, Medical Services in the Petroleum Industry.

Dr. Victor G. Heiser, New York, will speak at a luncheon of the section on industrial nursing on "Improving the Health of Industrial Workers," and Dr. Howard W. Haggard, New Haven, Conn., at a dinner of the New Jersey chapter, American Society of Safety Engineers and the engineering section, on "Poisonous Gases of Modern Industry."

FOREIGN

Contributions Requested in Honor of Dr. Schaumann.—In honor of Dr. Jörgen N. Schaumann, chief physician of the St. Görans Finsen Institute, Stockholm, Sweden, who celebrates his sixtieth birthday this year, a group of his friends and colleagues propose a jubilee number of *Acta medica Scandinavica*, with extracts from *Acta dermato-venereologica*. Twenty-five years has passed since Schaumann first submitted the work in which he showed that lupus pernio (Besnier) and Boeck's sarcoids were skin manifestations of a generalized disease which he called lymphogranuloma benignum or lymphogranulomatosis benigna. Owing to differences of opinion as to the suitability of this name, it was suggested in 1935 that the disease be called Schaumann's disease. Those who wish to contribute articles to the volume to honor Dr. Schaumann are requested to send their contributions to the editor of *Acta medica Scandinavica*, Prof. Israel F. Holmgren, Jacob Westinsgatan 4, Stockholm, before November 15.

Government Services

Examination for Navy Medical Corps

An examination for commission and for appointment as intern in the Medical Corps of the United States Navy will be held at all naval hospitals in the United States and at the Naval Medical School, Washington, D. C., beginning November 6. Candidates must be between the ages of 21 and 32 at the time of appointment and graduates of or senior medical students in recognized medical schools. Those interested should write the Surgeon General, U. S. Navy, Bureau of Medicine and Surgery, Navy Department, Washington, for further information.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 9, 1939.

The Annual Meeting of the British Association for the Advancement of Science

The imminence of war did not prevent the annual meeting of the British Association for the Advancement of Science, which was held at Cardiff.

A NEW APPROACH TO BIOLOGY

In his presidential address to the Section of Chemistry Prof. E. K. Pideal said that whereas toward the end of the last century the biologist was concentrating on the whole living unit of the cell, in this century the tendency has been for the study of the living unit to be dropped and in its place investigations to be made on particular processes such as oxidation and reduction. This change of approach, though it has produced many valuable results, inevitably leaves out of account the coordination of the separate activities of cells or cell assemblages. One of the chief characteristics of living matter is the presence both of material and of energy in the shape of films, membranes, fibrils and fine capillaries—a microstructure with a relatively huge surface. To do justice to this feature of life we need to study the properties of what biologists call interphases—the surfaces of separation between bulk phases of substance. We want to know more of the properties of "matter in the boundary state."

An analysis of the colloidal properties of living matter reveals that a large part of the material and energy lies in the interphase. The question arises: How far are physical and chemical reactions modified? The composition and structure of the interphase have been exhaustively examined in the last twenty years. Recent work has shown that the interphase often consists of what is called monolayer, a sheet of molecules only one layer thick. Much work has been done on the physical properties of the monolayers of the macromolecules such as protein and methylated cellulose and starches. These are of interest in that two dimensional gels, prototypes of membranes, can be formed. The fact that the molecules in monolayers are orientated in respect both to the substrate and to their neighbors and that the orientation can be affected by contraction or expansion of the monolayer has an important bearing on the reactions. Surface chemical reactions, including both enzyme activity and photochemical processes, are examples.

Since molecules at interfaces are orientated, molecules in the two component systems of different species can be adlineated with respect to one another. Complexes are formed by the penetration of a monolayer of one species by the molecules of the penetrant. These penetrative reactions appear to be involved in various biologic processes, such as lysis, agglutination and sensitization, and to play a part in the actions of various drugs.

Study of the properties of the interphase surface is throwing light on many biologic facts. It enables a theoretical interpretation to be given of the existence of bio-electrical potentials. The cancer producing hydrocarbons, examined by the monolayer technic, prove to be unreactive themselves but readily converted into extremely active and water soluble substances which are strongly lethal to paramecium, apparently because of the ease with which they attack protein monolayers. These monolayer studies may throw light on the cancer problem, as interphase studies are necessary for the construction of any model, however crude, of the mechanism of biologic organization and function.

PERSPECTIVES IN EVOLUTION

In the Section of Zoology the president, Prof. James Ritchie, devoted his address to perspectives in evolution. He said that investigation of the properties of living things has led to a modification of both the extremely mechanistic and the extremely vitalistic views of life and has gone far to reducing its mystery to terms of physics and chemistry. Theories of the cell as an electromagnetic unit of life and of life as a dynamic equilibrium between such units, or of life and the cell as originating in an ethereal vortex, are less convincing than the researches which show that certain activities of cells conform to the laws of osmotic systems, to Donnan's membrane equilibrium and to catalytic action brought about by enzymes. But none of these interpretations reach the ultimate secret of life. This is apparent in a perspective of evolutionary processes.

Living organisms have aggregated vast deposits of calcareous and silicious ooze from the dilute solutions of the ocean and have gathered great formation of coal from the tenuous stores of carbon dioxide in the atmosphere. This is something quite different from the normal progress of gases or solutions to maximum dispersal of their particles. Moreover, the evolution of life from the simple to the complex is an increase of orderly arrangement, apparently opposed to the thermodynamic law of increasing randomness. Living matter appears to hold up the physical course of the degradation of matter, if it does not actually reverse it, through its power of trading with the environment, so that it can build up stores of high potential energy from materials of lower potential.

Another recent development is the lengthening of perspective life on the earth. Newer knowledge of the ages of geological formation, based on the break up of radioactive minerals in the rocks, shows the extreme slowness of evolution and emphasizes the significance of man as an agent of change in the living world, for his active part in this process is virtually confined to our era and mainly to the last 300 years. In that insignificant period man has produced faunal changes in civilized lands comparable only to the great secular changes of world evolution.

The 1,200 million years through which life has been evolving lead to a view of man's future. His past is insignificant in time; his long future is unknowable as far as science is concerned. But bearing in mind the impetus of evolution, we can conclude that his progress will be continued toward perfection of social life and widening of the social idea to include nations as well as individuals. The history of life on the earth is opposed to the view that with the coming of man evolution would cease or be tied up for all time to trifling changes in brain power or better social organization. It suggests that man, so far the greatest manifestation of life on the earth, may be no more than a stage on the path of evolution to a greater future.

The Indian Journal of Surgery

The *Indian Journal of Surgery* is a new periodical published as an organ of the Association of the Surgeons of India. The opening editorial complains that the Indian practitioners "have been completely under the thumb of the Indian Medical Service" until quite recently and even now are not completely emancipated. While giving this great service credit for much original research, the writer does not mention that it introduced European medicine into India and that its many distinguished members created the greater part of tropical medicine. It is thanks to this service and the British government, whose instrument it is, that Indians have been educated in modern medicine.

The first number, of forty-eight pages, is devoted to the inaugural conference of the Association of Surgeons of India. In his presidential address Lieut.-Col. Gopinath Pandalai, F.R.C.S., of the Indian Medical Service, stated that the association had received the good wishes of the Association of the Surgeons of Great Britain and Ireland and that when he

visited Rochester the Mayos asked him to convey their cordial greetings. Only two subjects are reported from the conference —the treatment of ileocecal tuberculosis and carcinoma of the tongue. While showing nothing of original importance, the papers and discussions are quite up to the European level. This was to be expected, as several of the surgeons hold the highest qualification—the fellowship of the Royal College of Surgeons of England. The position attained by the Indian surgeons today is only one result of the British policy of elevating the peoples of the empire to the level at which they can rule themselves. Nothing comparable has ever been done by any other empire, ancient or modern.

BERLIN

(From Our Regular Correspondent)

Aug. 17, 1939.

Public Health in 1938

In the report of the public health service is information regarding public welfare. This information does not include lands acquired recently by conquest. Of those intending to marry, 47 per cent made use of public consultations (36 per cent in 1937). Of these, 38 per cent received a marital loan, that is to say an addition to the expenses incidental to getting established. Maternity advice was sought by 6 per cent of pregnant women. Infant welfare stations were available to the public in the ratio of one for seventy-seven infants born and were actually consulted on the average by sixty mothers per station. Consultation for preschool children was offered in the proportion of 718 per hundred thousand inhabitants. More than 3,000,000 children of school age received attention, that is, about 4,545 per hundred thousand inhabitants. The schools of almost all districts, with few exceptions, were furnished dental supervision.

The care of tuberculous patients was extended during 1938. About 1,500,000 patients, against 1,250,000 in 1937, received attention. The number of roentgen treatments rose from about 1,250,000 to about 1,750,000. Hospitalization in public institutions increased from 45,000 to 49,000. Average x-ray examinations were 100 to thirteen patients. Somewhat greater facilities were provided for the treatment of venereal diseases, but the number of individual cases decreased (192,000 in 1938 against 200,000 in 1937). Consultation stations for cripples were increased and, on the average, 242 persons were advised per hundred thousand inhabitants. The increase in stations for alcoholic persons is more than counterbalanced by the decrease of the individuals consulting. However, other agencies not identical with these cooperated in the care for alcoholic patients and their reports are not included in these figures. About 107,000 persons with psychic troubles were advised against 91,000 in 1937. The care for the infirm and aged is likewise organized according to regions. These facts should not be regarded as completely evaluating the achievements of public health welfare, because there are other agencies besides the official health stations connected with public health bureaus. At any rate, the facts presented give sufficient insight into the extensive nature of public welfare activities in operation in Germany.

Primary Infection with Tuberculosis in the Army

Dr. Hans Mayer has published the results of his investigations in the *Deutscher Militärarzt*. In the time between graduation from school (about 14 years) and military service (about 20 years of age) there is a huge gap in our knowledge of the tuberculin reaction. According to the literature, almost uniform results have been obtained from serial tuberculin inoculations in different European armies. From 15 to 20 per cent of those reporting for military training are free from tuberculosis. Mayer examined 600 soldiers in 1937, employing the Pirquet-Mantoux test, and obtained 84.33 per cent of positive reactions. No noteworthy difference was found between city, town and country recruits. Most of the 600 were natives of southern or southwestern Germany. With radiologic examination, seventy-eight showed a specific condition with positive reaction; sixty-seven (11.67 per cent) had a calcified primary complex. One must also consider that many of the recruits with negative reactions are increasingly susceptible, because of lack of previous exposure, and acquire primary infection during training. In most cases this infection does not lead to illness. The change from negative to positive reaction remains the only symptom. By means of careful selection of recruits for training and early recognition of the tuberculous, the army can be well protected against tuberculosis.

Epidemic Poliomyelitis in Frankfort on the Main

Dr. Windorfer has published his observations in the childrens' clinic of the university in Frankfort on the Main regarding 150 patients treated for this disease last year. The infection of infants, the higher mortality rate with increasing age and the greater prevalence among boys and girls (eighty-eight against sixty-two) were all typical. Ten of the 150 patients died, fifty-four had paralysis eight weeks after, and fifty-seven had recovered at the time of discharge from clinical care. In twenty-nine no paralysis had appeared at all. The treatment employed consisted (1) in the use of serum, (2) in the administration of vitamin B_1 and (3) complete rest. Forty children were treated with serums, 110 without. Comparison of results favored neither therapy. Six patients were given serum preparalytically; four of these remained free from paralysis, one acquired serious paralyses of a permanent nature and one died. Thirty-five patients were given ten injections of vitamin B_1 of 10 mg. each. In fifteen a gradual improvement set in, in nine a good involution, and in the other eleven no involution. No decisive effect of vitamin B_1, subcutaneously administered, can therefore be deduced. In lumbar punctures of fifteen patients with Landry's paralysis, observations gave the impression that vitamin B_1 resisted the advance of fatal paralyses. However, the final results (three deaths, ten serious paralyses of a permanent nature and two recoveries) constitute no evidence for a specific effect of vitamin B_1. For those acutely ill, complete rest was the best treatment.

Congress of Otorhinolaryngologists

In this year's meeting of the Congress of Otorhinolaryngologists in Vienna the two main topics were lupus and tumors of the acusticus. Prof. Alfred Stühmer of Freiburg, a pioneer in the systematic treatment of lupus, read the dermatologic paper. The main difficulty, he said, lay in applying the treatments at the right time and in the early stage of the disease. Statistics for the nation indicate 30,000 cases of lupus and clearly show that cases are reported only as individual districts possess good organizations. The important thing in treating patients was to continue therapeutic measures systematically until a complete cure had been effected. Much harm is done through incomplete measures. Lupus is only one form of cutaneous tuberculosis, though the most frequent. The organism possesses a certain resistance to each of these forms; for this reason mutation of one of these phenomena into another is rare.

Prof. Alfred Brüggemann of Giessen, an otorhinolaryngologist, stated that transitions into other forms of mucous membrane tuberculosis were quite common and that benign lesions often showed transition to those prognostically less favorable. It was not rare for a lupus carcinoma to bring about a slow and painful death. Prof. Johannes Zange of Jena pointed out that, contrary to former belief, such patients could be operated on. Radical surgical intervention could effect cures even in advanced destruction of the facial tissue and accessory nasal cavities. N. G. Riecke of Kiel discussed periarteritis nodosa of the mucosa of the nose from the point of view of differential

diagnosis. It begins with a simple cold and induces death within a few months by rapid destruction of cartilage and bone and the formation of slightly hemorrhagic granulations. Clinical observations in Münster during fourteen years proved the efficacy of roentgen rays with a dosage of 70 mg. to 1 mm. of zinc filtration per square centimeter in contact irradiation. He also called attention to the great curative value of vitamin C in treating tuberculous mucous centers.

L. Schönbauer, Viennese surgeon, treated the question of the surgical therapy of tumors of the acusticus. In fifty-six cases postoperative mortality amounted to 25 per cent; recovery, after three years, to 28 per cent. The surgeon, he said, gets access to the tumor by opening as broad as possible a path to the occipital cranial fossa. Güttich of Cologne stated that the results obtained by otologists corresponded to those mentioned. Otologists had two advantages in the surgery of these tumors, to proceed altogether or partially by way of the labyrinth or to utilize the experience gained in operating within narrow confines and thus to reduce the great danger of injury to the brain through displacement of the cerebellum.

Meeting of Balneologists

The meeting of the German society of balneologists and climatologists, with the inclusion of Austria and its alpine regions, is to make intensive studies of the curative possibilities of mountain altitudes. As Professor von Ficker of Vienna explained, climatologic values must be judged not only by solar radiation, which included warmth effects and solar wavelengths, but also by the humidity of the air, the winds and the oxygen content of alpine altitudes. Localities especially suitable for mountain resorts and sanatoriums are those possessing a high degree of dry air, though with somewhat higher temperature, and are found 300 meters above valley level even if the valley is foggy. Such air is favorable to tuberculous persons, whereas the healthy tourist seeking relaxation can utilize the strong stimulation of climate changes, passing from cool valleys to warmer and drier altitudes frequently within an hour.

The second chief topic concerned the comparison between natural medicaments and their artificial substitutes. Artificial climate produced in rooms does not constitute a sufficient substitute for the natural climate. Climatizing is valuable for operating rooms and in certain diseases but not for general application to hospitals and workshops. Quantitative differences were found in artificial products recommended for drinking treatments instead of natural waters; likewise the total absence of the effect was noted. In some cases an opposite effect was produced. Among the 900 artificial bath preparations examined, a few good ones were discovered among a host of inferior ones.

Marriages

ARTHUR J. VANDERGRIND, Assistant Surgeon Lieutenant, U. S. Navy, to Miss Pearlie Mae Arington of Uriah, Ala., in Daphne, May 25.

ALBERT E. AUSTIN, Old Greenwich, Conn., to Miss Lillian V. Lounsbury of Stamford, Conn., in Norfolk, Mass., September 3.

HJALMAR MORTENSBAK, Hanska, Minn., to Miss Muriel Swihart of Balaton in St. Paul, June 3.

MOLLEURUS COUPERUS, Chehalis, Wash., to Miss Florence Schmidt of Dickinson, N. D., July 19.

LOUIS FRANK LESSER, Mountain Home, Idaho, to Miss Mary Wolf of Delaware, Ohio, June 21.

HERMAN H. SCHOFFMAN, Seattle, to DR. LILY LEDERER of Vienna, Austria, June 22.

ROBERT H. WARD to Miss Nancy Stark, both of New York, June 24.

HUNTER J. MACKAY to Miss Leola Trotter, both of Seattle, June 24.

Deaths

John Alexander Donovan ✦ Butte, Mont.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1894; member of the American Academy of Ophthalmology and Otolaryngology and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; chairman of the Section on Ophthalmology of the American Medical Association, 1926-1927; past president of the Medical Association of Montana; member of the state board of medical examiners; chairman of the medical advisory board and member of the state board of National Defense during the World War; on the staff of St. James Hospital; aged 67; died, July 21, of mesenteric thrombosis.

Clarendon James Combs ✦ Oshkosh, Wis.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; fellow of the American College of Surgeons; served during the World War; retired in 1938 as commanding officer of the 370th medical regiment of the U. S. Reserve Officers Training Corps; aged 64; on the staffs of St. Mary's Hospital and the Mercy Hospital, where he died, July 19, of gallstones, acute hemorrhagic pancreatitis and myocarditis.

William Mortimer Brown, Rochester, N. Y.; University of the City of New York Medical Department, 1889; fellow of the American College of Surgeons; formerly on the staff of the Rochester General Hospital; past president of the Monroe County Medical Society; consultant in obstetrics and gynecology at the University of Rochester School of Medicine; aged 71; died, July 25, of illuminating gas poisoning, self administered.

Frederick Martin Bauer, Whitesboro, N. Y.; University of the City of New York Medical Department, 1886; member of the Medical Society of the State of New York; formerly medical superintendent in charge of the Tuberculosis Division, Metropolitan Hospital, Blackwell's Island, and deputy medical superintendent of the Kings County Hospital, Brooklyn; aged 79; died, July 4, of coronary thrombosis and arteriosclerosis.

William Arthur Toland, Houston, Texas; Jefferson Medical College of Philadelphia, 1911; member of the State Medical Association of Texas; fellow of the American College of Surgeons; served during the World War; on the staff of the Memorial Hospital; on the visiting staffs of St. Joseph's Infirmary, Methodist, Hermann and Houston Negro hospitals; aged 56; died, July 23.

Robert John McGuire ✦ Syracuse, N. Y.; Syracuse University College of Medicine, 1912; fellow of the American College of Surgeons; instructor of gynecology at his alma mater; on the staff of the Hospital of the Good Shepherd; served during the World War; aged 54; died, July 23, of coronary occlusion, chronic myocarditis and arteriosclerosis.

Edward Michael Dooley, Buffalo; Niagara University Medical Department, Buffalo, 1890; member of the Medical Society of the State of New York; on the staffs of the Emergency Hospital of the Sisters of Charity and the Mercy Hospital; aged 78; died, July 20, of diabetes mellitus, peritonsillar abscess, arteriosclerosis and chronic myocarditis.

Charles Walker Streamer ✦ Pueblo, Colo.; University of Colorado School of Medicine, Denver, 1916; past president of the Pueblo County Medical Society; served during the World War; fellow of the American College of Surgeons; aged 46; on the staffs of the Parkview Hospital and St. Mary's Hospital, where he died, July 5, of bronchopneumonia.

Frank Henry Carlisle ✦ Wellesley, Mass.; Harvard University Medical School, Boston, 1904; member of the American Psychiatric Association and the New England Society of Psychiatry; formerly medical director of the Bridgewater (Mass.) State Hospital; aged 59; died, July 20, in the Palmer Memorial Hospital, Boston, of carcinoma of the colon.

Alexander MacGillivray Young, Saskatoon, Sask., Canada; McGill University Faculty of Medicine, Montreal, Que., 1906; at one time mayor; formerly registrar Council of the College of Physicians and Surgeons of Saskatchewan and secretary of the Saskatchewan Medical Association; aged 60; died July 9, of brain tumor.

Henry Augustus Peters ✦ Oconomowoc, Wis.; Milwaukee Medical College, 1906; past president of the Waukesha County Medical Society; for many years member of the state board of pharmacy examiners; aged 66; on the staff of the Summit Hospital, where he died, July 19, of pulmonary embolism following an appendectomy.

Abraham Orenstein, New York; Long Island College Hospital, Brooklyn, 1910; member of the Medical Society of the State of New York; served during the World War; on the

staffs of the New York Polyclinic Hospital and the Veterans Administration Facility; aged 51; died, July 13, of arteriosclerosis and hemiplegia.

David Fitch Armstrong, Auburn, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1895; member of the Medical Society of the State of New York; formerly on the staff of the Auburn City Hospital; aged 70; died, July 31, of cerebral hemorrhage.

Vincent Joseph Irwin, Springfield, Mass.; University of Vermont College of Medicine, Burlington, 1896; member of the Massachusetts Medical Society; member of the American Academy of Ophthalmology and Otolaryngology; aged 81; died, June 19, in Tampa, Fla., of chronic nephritis and arteriosclerosis.

Charles W. Polk, Memphis, Tenn.; Memphis Hospital Medical College, 1902; member of the Tennessee State Medical Association; formerly in charge of child hygiene work for the board of health of Shelby County, and health officer of Lauderdale County; aged 59; died, July 5, of cerebral thrombosis.

Charles Floyd Stafford, Cle Elum, Wash.; Northwestern University Medical School, Chicago, 1913; member of the Washington State Medical Association; at various times city and county health officer; aged 52; died, July 6, in the Swedish Hospital, Seattle, of staphylococcic septicemia.

James Egbert McClelland Roberts, Charleston, W. Va.; University of Louisville (Ky.) School of Medicine, 1925; member of the West Virginia State Medical Association; on the staff of the Mountain State Hospital; formerly county coroner; aged 40; died, July 25, in Collierstown, Va.

Arthur Henry Miller, Denver; University of Colorado School of Medicine, Denver, 1923; member of the Colorado State Medical Society; on the staffs of the Denver General, Children's, Presbyterian, St. Luke's and Porter hospitals; aged 56; died, July 25, of coronary thrombosis.

Peter H. Stockfleth, Cameron, Mo.; Eclectic Medical Institute, Cincinnati, 1905; Barnes Medical College, St. Louis, 1906; served during the World War; formerly on the staff of the Western Oklahoma Hospital, Supply; aged 59; died, July 5, of a self-inflicted bullet wound.

Harry C. Tull, Salisbury, Md.; University of Maryland School of Medicine, Baltimore, 1900; member of the Medical and Chirurgical Faculty of Maryland; on the staff of the Peninsula General Hospital; aged 65; died, July 17, in Ocean City of coronary thrombosis.

Howard Birch Pedigo ✠ Beaumont, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1902; served during the World War; on the staffs of the Hotel Dieu Hospital and St. Therese Hospital; aged 61; died, in July, of a self-inflicted bullet wound.

G. Thomas Lee Bryan, Abilene, Texas; American Medical College, St. Louis, 1908; member of the State Medical Association of Texas; veteran of the Spanish-American War; aged 62; died, July 28, in the Veterans Administration Facility, Waco, of cerebral arteriosclerosis.

Adalbert Jerome Cole, Clear Lake, Iowa; Rush Medical College, Chicago, 1883; member of the Iowa State Medical Society; formerly mayor of Britt, councilman and member of the school board; aged 86; died, July 17, in Mason City of arteriosclerotic nephritis.

William Charles Porath ✠ Storm Lake, Iowa; Hahnemann Medical College and Hospital, Chicago, 1902; Denver and Gross College of Medicine, 1903; president of the Buena Vista County Medical Society; aged 66; died, July 18, of coronary occlusion.

Henry Fletcher Long ✠ Statesville, N. C.; University of Maryland School of Medicine, Baltimore, 1892; fellow of the American College of Surgeons; surgeon to a hospital bearing his name; aged 70; died, July 28, of hypostatic pneumonia and erysipelas.

James Bryant Person, Selma, N. C.; Medical College of Virginia, Richmond, 1897; member of the Medical Society of the State of North Carolina; past president of the Johnston County Medical Society; aged 65; died, July 16, of lymphosarcoma.

Walter Landor Savage, Buffalo; Niagara University Medical Department, Buffalo, 1897; veteran of the Spanish-American War; formerly on the staff of the U. S. Marine Hospital; died, July 24, of chronic myocarditis and arteriosclerosis.

James Charles Sharkey, Rensselaer, N. Y.; Albany Medical College, 1896; school physician; formerly county coroner and health officer of Rensselaer; on the staff of St. Peters Hospital; aged 70; died, July 5, of cerebral thrombosis and arteriosclerosis.

Richard Stephen MacCabe, Oklahoma City; University of Missouri School of Medicine, Columbia, 1906; member of the Oklahoma State Medical Association; on the staff of St. Anthony Hospital; aged 56; died in July of rheumatic heart disease.

Harry Wolf Nye, Osborne, Kan.; College of Physicians and Surgeons, Keokuk, Iowa, 1895; Drake University Medical Department, Des Moines, Iowa, 1897; member of the Kansas Medical Society; aged 66; died, July 6, of nephritis and myocarditis.

Arthur Heath Flickwir ✠ Fort Worth, Texas; University of Pennsylvania Department of Medicine, Philadelphia, 1901; health officer of Houston, 1920-1929; for many years director of public health and welfare of Fort Worth; aged 60; died, July 26.

Joseph Matthew Griffith ✠ Tyler, Texas; Baylor University College of Medicine, Dallas, 1918; formerly secretary of the Smith County Medical Society; on the staff of the Mother Frances Hospital; aged 49; died, July 28, in Midland.

Lea Hume, Eagle Pass, Texas; University of Texas School of Medicine, Galveston, 1902; acting assistant surgeon, U. S. Public Health Service; aged 63; died, July 27, of injuries received when the horse he was riding was struck by a truck.

Joseph Edwin Slicer, Shreveport, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1901; member of the Louisiana State Medical Society; served during the World War; aged 59; died, July 15, of cerebral hemorrhage.

Arthur Burke O'Brien ✠ Rochester, N. Y.; University of Buffalo School of Medicine, 1921; on the staff of St. Mary's Hospital; aged 43; died, July 6, of injuries received when the automobile in which he was driving was struck by a train.

Ernest Lawrence Perri ✠ Monaca, Pa.; Jefferson Medical College of Philadelphia, 1921; physician for the board of health of Monaca and school board; on the staff of the Rochester (Pa.) General Hospital; aged 41; died, July 9.

Charles Edward Thompson, De Funiak Springs, Fla.; Faculty of Medicine of Trinity College, Toronto, Ont., Canada, 1886; L.R.C.P., Ireland, 1886; aged 80; died, July 21, in a hospital at Pensacola of carcinoma of the prostate.

Philippe Auguste Charette, Montreal, Que., Canada; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1917; served during the World War; aged 46; died, July 14.

John H. Hereford, Colorado Springs, Colo.; St. Joseph (Mo.) Hospital Medical College, 1882; member of the Colorado State Medical Society; on the staff of the Beth-El Hospital; aged 77; died, July 27, of cerebral hemorrhage.

Frederick Fulton Tucker ✠ Nacogdoches, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1924; on the staff of the City Memorial Hospital; aged 39; died, July 29, of a self-inflicted bullet wound.

Levings A. Opdyke, Jersey City, N. J.; New York Homeopathic Medical College, 1885; member of the Medical Society of New Jersey; aged 77; died, July 6, of chronic endocarditis and a fractured hip received in a fall.

Henry Joy Francis, Troy, Ohio; Ohio State University College of Medicine, Columbus, 1939; aged 24; intern at St. Elizabeth Hospital, Dayton; was found dead, July 4, of incised wounds of the wrists, self inflicted.

James Oscar Ristine, Maquoketa, Iowa; State University of Iowa College of Medicine, Iowa, 1896; member of the Iowa State Medical Society; aged 73; died, July 14, in St. Luke's Hospital, Davenport, of acute nephritis.

Willis Edwards Lowry Sr., Laredo, Texas; College of Physicians and Surgeons, Baltimore, 1892; member of the State Medical Association of Texas; aged 69; died, July 29, in the Santa Rosa Infirmary, San Antonio.

Hugh Gilmer Welpton ✠ Des Moines, Iowa; Drake University Medical Department, Des Moines, 1897; formerly a medical missionary; aged 68; died, July 3, in the Baylor University Hospital, Dallas, Texas.

Robert L. Cox ✠ Houston, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1899; aged 63; on the staff of the Memorial Hospital, where he died, July 9, of carcinoma of the pancreas.

Wayne Paul O'Brien, Hot Springs, S. D.; University of Illinois College of Medicine, Chicago, 1911; aged 50; on the staff of the Veterans Administration Facility, where he died, July 25, of angina pectoris.

Louis Reich, Newark, N. J.; Medico-Chirurgical College of Philadelphia, 1906; veteran of the Spanish-American War; on the staff of the Beth Israel Hospital; aged 58; died, July 13, of cerebral hemorrhage.

Wilbur Fisk Thomson, Houston, Texas; University of Arkansas School of Medicine, Little Rock, 1938; on the staff of the Wright Clinic and Hospital; aged 27; was drowned, July 30, at Galveston.

John W. Leininger ✠ Gladwin, Mich.; Western University Faculty of Medicine, London, Ont., Canada, 1891; formerly mayor and president of the school board; aged 82; died, July 9, of chronic thrombosis.

Clarence Lee Crawford Atkeson, Columbia, Ala.; College of Physicians and Surgeons, Baltimore, 1884; member of the Medical Association of the State of Alabama; aged 78; died, July 14, of peritonitis.

William Lee Simpson, Wellsburg, W. Va.; Western Pennsylvania Medical College, Pittsburgh, 1902; member of the West Virginia State Medical Association; aged 64; died, July 15, of coronary thrombosis.

William Duncan Lockwood, Portland, Ore.; University of Missouri School of Medicine, Columbia, 1893; member of the Oregon State Medical Society; aged 70; died, July 18, of coronary occlusion.

Frank Morris Biddle ✠ Battle Ground, Ind.; Fort Wayne College of Medicine, 1895; county health officer; aged 65; died, July 27, 1939, in St. Elizabeth Hospital, La Fayette, of pulmonary fibrosis.

Pasquale Edoardo Maiello, Providence, R. I.; College of Physicians and Surgeons, Boston, 1922; Tufts College Medical School, Boston, 1923; served during the World War; aged 41; died, July 19.

Frederick Jacob Haendel, New York; University of Vermont College of Medicine, Burlington, 1898; aged 73; died in June in St. Luke's Hospital of arteriosclerosis, myocarditis and nephritis.

George Weldon Oliver, Medina, Tenn.; University of Nashville Medical Department, 1900; member of the Tennessee State Medical Association; aged 70; died, July 9, of coronary occlusion.

Edgar Palmer Peake, Oshkosh, Wis.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1900; served during the World War; aged 64; died, July 27, of coronary occlusion.

George Wilton Moorehouse, Cleveland; Harvard Medical School, Boston, 1897; formerly chief of the city bureau of communicable diseases; aged 72; died, July 14, of carcinoma of the pancreas.

George Regard Beridon, Opelousas, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1915; member of the Louisiana State Medical Society; aged 48; died, July 27.

William Breen, Oxford Junction, Iowa; State University of Iowa College of Medicine, Iowa City, 1908; aged 56; died, July 24, in a hospital at Iowa City of urethral stricture and rupture.

John Bennett Townsend ✠ Anderson, S. C.; University of Virginia Department of Medicine, Charlottesville, 1896; on the staff of the Anderson County Hospital; aged 68; died, July 13.

Henry Lazaar, Memphis, Tenn.; University of the South Medical Department, Sewanee, 1901; aged 61; died, July 30, in St. Joseph's Hospital of arteriosclerosis and coronary thrombosis.

James Beverly De Shazo, Ridgeway, Va.; Bellevue Hospital Medical College, New York, 1892; member of the Medical Society of Virginia; aged 70; died, July 31, of coronary occlusion.

Alphonse J. Kennedy Genella, Kenner, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1895; president of the parish board of health; aged 67; died, July 11.

Edmond Ray Keith, Lawrence, Kan.; American Medical College, St. Louis, 1891; member of the Kansas Medical Society; aged 75; died, June 29, in the Lawrence Memorial Hospital.

Barnard Tillman Bridges, Hartford, Ala.; University of Alabama School of Medicine, 1909; member of the county school board; aged 55; died, July 18, in a hospital at Dothan.

Warner Latta Crouch ✠ Fairview, Ill.; Rush Medical College, Chicago, 1912; served during the World War; aged 54; died, July 21, in the Graham Hospital, Canton, of uremia.

David C. Wylie Jr. ✠ Aspermont, Texas; Baylor University College of Medicine, Dallas, 1928; aged 39; died, July 5, of pneumonia as the result of a self-inflicted bullet wound.

Charles J. Kehm, Newport, Ky.; Eclectic Medical Institute, Cincinnati, 1896; member of the Kentucky State Medical Association; formerly health officer; aged 70; died, July 12.

Thomas Taylor Cosgrove, Sylvania, Ohio; Northwestern Ohio Medical College, Toledo, 1888; aged 78; died, July 29, in a hospital at Toledo following an automobile accident.

Fielding G. Carroll, Cave City, Ky.; University of Louisville School of Medicine, 1910; member of the Kentucky State Medical Association; aged 58; hanged himself, July 7.

Randolph McCutcheon, South Charleston, W. Va.; Medical College of Virginia, Richmond, 1924; served during the World War; aged 48; died, July 28, of coronary thrombosis.

Louise Di Moja, New York; New York Medical College and Hospital for Women, New York, 1907; aged 54; died, July 5, in Long Branch, N. J., of coronary occlusion.

William Henry Hinklin, Marion, Ohio; Eclectic Medical Institute, Cincinnati, 1891; formerly county coroner; aged 81; died, July 27, in Columbus of organic heart disease.

Lynn Arthur Martin, Binghamton, N. Y.; New York Homeopathic Medical College, New York, 1886; aged 74; died, July 20, of diabetes mellitus and angina pectoris.

John Calhoun Wilkins, Beekman, La.; Memphis (Tenn.) Hospital Medical College, 1892; aged 72; died, July 22, in a hospital at Bastrop of cerebral hemorrhage.

Charles Monroe Campbell, Ralph, Ala.; University of Tennessee Medical Department, Nashville, 1894; aged 72; died, July 22, of carcinoma of the prostate.

Oscar Bernard Payne, Chicago; Chicago Medical School, 1923; aged 50; died, July 3, in the Provident Hospital of pulmonary embolism from thrombophlebitis.

Tully M. Talbot, Valdosta, Ga.; Columbus Medical College, 1888; member of the Medical Association of Georgia; aged 79; died, July 9, in Austin, Texas.

Ellis Charles Brown, Portland, Ore.; University of Michigan Homeopathic Medical School, Ann Arbor, 1880; aged 86; died, July 1, in the Emanuel Hospital.

William J. Wick, Chicago; Rush Medical College, Chicago, 1890; member of the Illinois State Medical Society; aged 72; died, July 29, of chronic myocarditis.

Henry C. Holtzendorff, Mishawaka, Ind.; Medical College of Indiana, Indianapolis, 1895; formerly county coroner; aged 68; died, July 30, of heart disease.

Bruce Blance Mitchell, Tuscaloosa, Ala.; Meharry Medical College, Nashville, Tenn., 1903; aged 53; died, July 24, of mitral lesion with decompensation.

John Cantzon Foster, Tampa, Fla.; Medical College of Virginia, Richmond, 1901; aged 63; died, July 22, in Timmonsville, S. C., of lobar pneumonia.

Henry Jones, Coolidge, Ga.; Atlanta Medical College, 1895; member of the Medical Association of Georgia; aged 68; died, July 7, at Milledgeville.

Aaron Friedman, Hoboken, N. J.; Jefferson Medical College of Philadelphia, 1902; aged 75; died, July 14, at the Mount Sinai Hospital, New York.

Edward Patrick Philbin, Buffalo; University of Buffalo School of Medicine, 1922; aged 41; was drowned, July 7, when his motor boat capsized.

Janet Leah Long-McCollum, Oak Park, Ill.; Illinois Medical College, Chicago, 1896; aged 79; died, July 30, of carcinoma of the uterus.

Harry Lawrence Rubin, Chicago; Loyola University School of Medicine, Chicago, 1922; aged 43; died, July 5, of rheumatic heart disease.

Benjamin Tappan Loring ✠ Watertown, Mass.; Boston University School of Medicine, 1898; aged 70; died, July 29, of coronary heart disease.

Arthur J. Childress ✠ Jefferson, Texas; Eclectic Medical University, Kansas City, Mo., 1915; aged 56; died, July 29, of coronary occlusion.

Don Wilson Vanderhoof, Omaha; Creighton University School of Medicine, Omaha, 1913; aged 52; died, July 28, of Hodgkin's disease.

Henry Wasson Baskette, St. Louis; University of Nashville (Tenn.) Medical Department, 1882; aged 78; died, July 15, of carcinoma.

Alfred Merritt Sorell ✠ Baltimore; College of Physicians and Surgeons, Baltimore, 1907; aged 57; died, July 21, of pyelonephrosis.

William H. Wethers, Baton Rouge, La.; Meharry Medical College, Nashville, Tenn., 1910; aged 57; died, July 20, in New Orleans.

William Hunter Haw, Atlanta, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1928; aged 36; died in July.

Armand Lafleur, Lawtell, La.; Louisville (Ky.) Medical College, 1889; aged 68; died, July 11, of cardiac decompensation and pellagra.

Charles Alvin Portz ✠ Canton, Ohio; Ohio Medical University, Columbus, 1905; aged 62; died, July 10, of coronary thrombosis.

Edmund Burke Hardin, Lakeland, Fla.; Louisville (Ky.) Medical College, 1896; aged 65; died, July 8, of carcinoma of the larynx.

Charles Franklin Bryan, Corsicana, Texas (licensed in Texas under the Act of 1907); aged 64; died, July 5, of coronary occlusion.

Charles Lewis Crow, Columbus, Ky.; St. Louis College of Physicians and Surgeons, 1908; aged 71; died, July 18, of carcinoma.

Joseph Sterling Yount, Chicago; Rush Medical College, Chicago, 1893; aged 72; died, July 17, in the Illinois Central Hospital.

Max L. Rich, Grand Island, Neb.; Omaha Medical College, 1893; aged 68; died, July 18, of chronic myocarditis and hypertension.

Irving Layton Drake, Durant, Okla.; Gate City Medical College, Dallas, Texas, 1907; aged 59; died, July 21, of a heat stroke.

William H. Emery, Lorain, Ohio; Toledo Medical College, 1898; veteran of the Spanish-American War; aged 65; died, July 19.

Joseph Etienne Germain, Rimouski, Que., Canada; Laval University Faculty of Medicine, Quebec, 1913; aged 52; died, July 3.

Elmer C. Hanson ✠ Austin, Minn.; University of Minnesota Medical School, Minneapolis, 1922; aged 42; died, June 23.

Chando H. Malcolm, Huntington, W. Va.; University of Louisville (Ky.) Medical Department, 1892; aged 68; died, July 17.

James D. Meadow, Sherman, Texas; Pulte Medical College, Cincinnati, 1891; aged 77; died, July 14, of heart disease.

F. H. Blount, Snow Hill, N. C. (licensed in North Carolina in 1885); aged 83; died, July 29, of coronary occlusion.

Olafur Stephenson, Winnipeg, Man., Canada (licensed in Manitoba in 1895); aged 74; died, July 17, of pelvic abscess.

Charles John Wood ✠ Genoa, Ohio; St. Louis University School of Medicine, 1933; aged 35; died suddenly, July 10.

Nicholas Boniface Pautler, Waterloo, Ill.; Missouri Medical College, St. Louis, 1893; aged 67; died, July 18.

Joseph R. Conyers, Gates, Tenn.; Memphis Hospital Medical College, 1888; aged 77; died, July 9, of pneumonia.

John Thomas Norman, Sharon, Miss.; Memphis (Tenn.) Hospital Medical College, 1894; aged 73; died, July 15.

David Thomas White, Blackford, Ky.; Kentucky School of Medicine, Louisville, 1885; aged 80; died, July 28.

Charles Forrest Alexander, Gratz, Ky.; Kentucky School of Medicine, Louisville, 1893; aged 70; died, July 26.

Abner Dale Neely, Lynch, Neb.; Marion-Sims College of Medicine, St. Louis, 1900; aged 80; died, July 23.

Elmer Newkirk Funk ✠ Shreve, Ohio; Starling Medical College, Columbus, 1903; aged 60; died, July 19.

Charles Pelham Ward, Atlanta, Ga.; Southern Medical College, Atlanta, 1894; aged 69; died, July 30.

James Coleman Fisher, Jefferson, Ohio; Rush Medical College, Chicago, 1889; aged 80; died, July 21.

Abram Jay Hansberry, Ozark, Ark. (licensed in Arkansas in 1903); aged 75; died, July 31, of sarcoma.

Harvey Dorman Kemper, Jonesboro, Ga.; Atlanta School of Medicine, 1909; aged 60; died, July 14.

Edward C. Duddy, Indianapolis; Hering Medical College, Chicago, 1899; aged 72; died, July 2.

William A. Musmann, Denver; Denver Homeopathic College, 1901; aged 74; died, June 22.

Bureau of Investigation

ANOTHER BRINKLER FRAUD ORDER

Long Time Diet Faker Is Once More Debarred from the Mails

The issuance of a Post Office fraud order against George H. Brinkler, of Miami Beach, Fla., on Oct. 21, 1938, and the release of a "cease and desist" order by the Federal Trade Commission on May 27, 1939, against the same individual, recall the many instances in which this self-styled "food expert" has had the rather dubious distinction of receiving the attention of the federal authorities.

For nearly thirty years Brinkler's meanderings in the diet field have been followed by the Bureau of Investigation of the American Medical Association. A case in which the Post Office Department declared the business of Brinkler (then operating from Washington, D. C.) to be fraudulent, obtained an indictment against him and debarred him from the use of the mails was reviewed in THE JOURNAL, Oct. 3, 1914. The government investigation had revealed Brinkler's literature as representing that his diet advice would, if followed, cure all diseases including even cancer, diabetes and Bright's disease. Brinkler has also claimed that certain foods cause tumors, coughs or catarrh to disappear, that too much cream, butter and cheese produce deafness and discharging ears, and that some foods make one nervous, whereas others bring about "the finest quality of Vitality, Electricity, Magnetism or Intelligence."

REMEMBER MY ADDRESS IN THE HOUR OF APPROACHING DEATH

IF you do not write now, be sure to put this booklet away carefully for future reference when sickness suddenly attacks you or your friends. I will send you another copy, to hand to a friend, if you let me know.

To remember my name and address may save valuable lives! When suddenly taken ill, you will not be scared to death through ignorance of the cause of your disease, but an intelligent self-confidence will make you hopeful as soon as you have learned the cause and cure of your attack.

Remember, when doctors despair of your life, in the hour of approaching death, that vital or brainy foods have restored the dying to robust health with the help of a competent teacher.

Read my testimonials attentively! They prove my efficiency in the cure of disease by vital or brainy foods.

Invitation to a Food Talk

Mrs. Mortimer, 33 Norwood Road, Shipley, Yorkshire, England, wishes me to state that she will be pleased to see any of my English and American correspondents who would like to have a talk with her or her husband about the brainy food system. Mr. Mortimer was rescued from the grave by Leppelloni some years ago. It always gives him great pleasure to relate his experience on the Leppel diet, which he began one evening, just after doctors had relinquished all hope of recovery. His family had been informed that he would not live through the night. His successful cure created a great sensation at the time, as he is well known in Yorkshire. All the members of the family have since adopted Leppelloni and enjoy excellent health.

This booklet must be enclosed as an introduction when writing for an interview.

G. H. BRINKLER
FOOD EXPERT
WASHINGTON. D. C.

Some of Brinkler's advertising of over twenty-five years ago.

The suckers who sent 10 cents for Brinkler's "valuable instructive booklet" entitled "The New Brainy Diet System" found that, instead of giving advice on diet, it was merely a come-on to get them to invest in Brinkler's "course." The booklet consisted largely of endorsements including one from a prolific producer of fake analyses and worthless testimonials. Further, Brinkler played up "scare stuff," such as "Remember my Address in the Hour of Approaching Death." With his booklet Brinkler sent out a "Question List" blank, to be filled out by the recipient and returned to Brinkler with $1. At least in some replies, Brinkler declared that the various disorders listed in the "answers" were due to improper diet. If one wanted to know just what constituted proper diet, he usually was asked to send Brinkler $40, $60 or $75, as the case might be.

On May 22, 1914, Brinkler was called on to show cause why a fraud order should not be issued against him. After a continuance had been granted him the hearing of the charges began and continued for ten days. Brinkler was then allowed three weeks in which to file a brief which, when submitted, was followed by an additional one and further evidence. These were carefully reviewed by the Solicitor for the Post Office Department, who brought out these facts: That in one case symptoms that might have been due to carcinoma of the stomach were "diagnosed" by Brinkler as due to improper diet; that another case, suggesting serious disease of the uterus, a further one indicating syphilis and one described as a well developed case of diabetes in a 12 year old boy were all diagnosed by Brinkler as due to faulty diet. Apparently Brinkler was giving the same

report in all cases, no matter how serious. Further, it was brought out that Brinkler was not a Doctor of Medicine, had no education in medical subjects and that girl clerks also lacking in medical knowledge used "form" paragraphs tabulated under symptoms in formulating replies to inquiries.

It was further shown that, when a woman wired Brinkler for advice in the case of an overgrown boy suffering from acute pulmonary tuberculosis involving both lungs, Brinkler asked her to wire $40 "for quick relief followed by complete course." The woman sent the money and received instructions as to what food the boy should and should not have. Soon afterward the boy was taken to a sanatorium and died. In spite of the mother's destitute circumstances, Brinkler refused to make any refund. This case was only one piece of evidence brought against Brinkler, leading up to the issuance of a fraud order against him on Aug. 19, 1914.

This did not, however, end the matter, for Brinkler contested the order and on Jan. 16, 1917, following a trial lasting three weeks, and after a twenty hours deliberation by a jury, Brinkler was acquitted of the criminal charge of using the mails to defraud. Involved in this decision, of course, was the difficulty confronting the prosecuting attorney of proving to the unanimous satisfaction of all the jurors not only that Brinkler's claims were false but that Brinkler *knew they were false*. Nevertheless, as the fraud order denying him the use of the mails still held, Brinkler applied for a ruling to set aside this disbarment but his appeal was denied. It is worth noting that in April 1915 and May 1916 the fraud order had been extended to cover the names of certain obscure individuals who appeared to be continuing this business under different titles.

For a time thereafter Brinkler was said to advertise in the newspapers of Washington, D. C., where he was located, and it appears that his business was limited to the readers of those papers and that they had to come to him as he advertised his office hours. Apparently, however, he finally decided to flout the Post Office fraud order, for in 1919 he was advertising from Atlantic City as the "Brinkler Institute." Around 1921 and apparently up into 1932 he was heard from in New York City, operating variously under the names "Brinkler School of Eating," "Brinkler Institute" and "Brinkler School and Dining Rooms" and his advertising indicated that he was using the mails. Some of his New York circulars announced him as "Manager" and named as the "Medical Director" one W. Wallace Fritz, who, although holding the degree of M.D., has helped promote various kinds of quackery and pseudomedicine and appears to have claimed "degrees" in chiropractic, osteopathy and some other things.

As many quacks and faddists move on to warmer climes in the winter, when business is good there, it is not surprising that in 1933 Brinkler was heard from at Miami Beach, where he was reported to be running a "Brinkler Institute."

The Post Office Department entered the picture again on March 25, 1938, when it called on the Brinkler Institute, the Brinkler School of Eating, "Dr." George H. Brinkler, J. Collins, F. Schumann and their officers and agents as such to show cause on May 4, 1938, why a fraud order should not be issued against them. Brinkler's attorney applied for an adjournment of the hearing for ninety days but the application was denied. Brinkler himself then asked for and obtained a postponement of at least a month. On May 26 Brinkler appeared at the hearing with a new attorney, who at the close of the testimony asked for a continuance until June 6, which was granted. On that date Brinkler came to the hearing without his attorney, Mr. Rowan, and the court put on record a telegram it had received from Rowan stating that he would not come to Washington to represent Brinkler further until the latter made satisfactory financial arrangements with him. Brinkler was thereupon granted a further continuance of one day to secure other counsel.

The hearing duly opened on June 7 and continued for five days. The Post Office reviewed the previous fraud order against Brinkler and its two extensions to cover other names. Further, it showed that in February 1927 Brinkler had been convicted in New York City on the charge of practicing medicine without a license and sentenced to spend six months in the workhouse or to pay a fine of $500. He chose to do the latter. In June of that year the appellate division of the New York Supreme Court upheld the sentence.

The Post Office also brought out that Brinkler had been representing that he could cure arthritis, gallstones, tuberculosis, tumors, cancer, diabetes, hardening of the arteries, high blood pressure, uterine disorders, apoplectic strokes and some other things; that there was "No Knowledge of Nutrition Without Brinklerism"; that "100% Improvements in 30 Days in Our Dining Room" were "guaranteed"; that "Dr. Brinkler is the oldest, most experienced, daringly original experimentalist in nutrition anywhere . . . has taught over 50,000 students, 99% successes"; and that he "lived over 35 years without drinking water."

The Post Office also showed that, whereas the "student" or "patient" paid a $30 fee for a course of "lessons" which purported to eliminate and cure disease by dietary rules that were represented as "individualized" to suit the particular case, these actually were mimeographed in form and generalized in content. The government introduced witnesses of high standing in the scientific world who discredited Brinkler's theories and claims.

Brinkler's first witness was a Fred W. Collins of Newark, N. J., naturopath and osteopath, whose testimony disclosed that he was not thoroughly familiar with Brinkler's methods and that these were substantially different from the ones he (Collins) used. Collins's testimony, it was said, further revealed that he possessed only a limited knowledge of dietetics.

Brinkler's second witness was introduced as Dr. George Joseph of Morgantown, W. Va., who testified that he was cured of diabetes by following Brinkler's treatment, though he could not explain the how or the why thereof. He admitted that his only knowledge of Brinkler's tenets was obtained through a reading of the latter's book, "Foresight—Foundation of Fortune," which the government showed to be essentially a book about social and economic conditions! Furthermore, from the evidence, the Post Office expressed serious doubt that the witness had ever had diabetes at all. Dr. Joseph received a diploma from the Eclectic Medical Institute, Cincinnati, in 1890 and a West Virginia license under the "years of practice" act. He is not a member of his local society or of the American Medical Association.

Then there was testimony offered for Brinkler by George E. Crandall of York, Pa., which was described in the Post Office report as "evasive and contradictory," in that this witness admitted he was not familiar with the dietary offered by Brinkler. The government report of the hearing commented that "Dr. Crandall's methods seem to be epitomized in his remark that although not subscribing to orthodox views he makes orthodox examinations to 'more or less fool the people.'" Crandall appears to be an osteopath and was himself requested by the Federal Trade Commission in 1938, when trading as "Dr. Crandall's Standard Institute," to discontinue making certain false claims for the alleged results of his mail-order "course in natural therapeutics."

Two lay witnesses also were presented by Brinkler but apparently did not help his case. Brinkler himself, though present at all the hearings, did not testify in his own behalf. He did obtain permission to file a brief. In this he lengthily expounded his views, which the Post Office Department could not consider seriously as he had been given ample opportunity to state his case during the hearings. His brief was reported to be largely a tirade against scientific medicine and a defense of the "naturopathic school of healing," all of which was beside the point as the government had neither defended the former nor attacked the latter. The proceedings brought out the fact that though Brinkler claimed to be a licensed naturopath his system did not conform to the naturopathic teachings, most of which, in fact, he appeared to repudiate. Also emphasized was the man's fundamental ignorance of the science of dietetics and nutrition as indicated by his attitude toward the scientific chemical analysis of foods into protein, carbohydrate and fat, which he termed ridiculous. In view of these and other facts the fraud order was issued against him on Oct. 21, 1938.

Meanwhile another government agency had taken cognizance of Brinkler's fakish claims. On Nov. 29, 1935, the Federal Trade Commission issued a complaint against George Henry Brinkler, operating from Miami Beach, Fla., under such names as "Brinkler School of Eating," "Brinkler School of Food Science," "Brinkler School of Nutrition" and "Brinkler Institute." Among the misrepresentations charged against the man

were that his correspondence course provided a competent treatment for all diseases and that his outlined method of diet was adequate for any of the thirty-six disorders listed, including indigestion, bronchitis, tuberculosis, hardening of the arteries and many others. Finally, on May 27, this year, the commission definitely ordered Brinkler to cease making the false representations named and some others, such as that persons who took his "courses" would achieve improved memory and eyesight, normal circulation, doubling of brain or muscle power, and a few other marvelous results.

Whether, in view of the fraud order of last October, Brinkler already had ceased to advertise and had discontinued his business by the time the Federal Trade Commission's order was issued is not evident, but if one may judge by his persistence in defying the original fraud order of 1914 he will be heard from again some of these days. In the meantime it is earnestly hoped that the public becomes slightly acquainted with the barest elementary facts concerning diet and nutrition, for that would be sufficient information to enable one to recognize Brinkler's folderol as fakery.

MISBRANDED "PATENT MEDICINES"

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE.—The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the composition; (4) the type of nostrum; (5) the reason for the charge of misbranding, and (6) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

Brown's Nosopen.—Am-Bro Co., Lawton, Okla. Composition: "Treatment No. 1," essentially water with small amounts of ephedrine sulfate and chlorbutanol; "Treatment No. 2," essentially mineral oil with small amounts of ephedrine and volatile oils, including those of eucalyptus and camphor. Fraudulently represented as a cure for hay fever, asthma, nasal catarrh and sinus headaches.—[*N. J. 28737; November 1938.*]

Diatine.—Scheidemann Remedy Co., Milwaukee. Composition: Essentially a coarsely ground plant material, chiefly juniper wood, bark, needles and berries, and small amounts of bearberry and senna leaves. Fraudulently represented as a treatment for diabetes.—[*N. J. 28739; November 1938.*]

Exanthum Oil.—William H. Trentlage, Elgin, Ill. Composition: An oily liquid containing fixed oils resembling those of olive and croton. Fraudulently represented as a remedy for sinus trouble, infected tonsils, appendicitis, toothache, rheumatism, etc.—[*N. J. 28982; November 1938.*]

Ferro China-Tonico Tessitore.—Tessitore's Chemical Mfg. Co., Inc., Providence. Composition: Essentially alkaloids of cinchona and a small amount of iron and ammonium citrate, with arsenic, saccharin, alcohol and water. Fraudulently represented as a remedy for fevers and a cure for headache, nausea, anemia, etc.—[*N. J. 28708; November 1938.*]

Flu-Go Mutton Suet.—Keystone Laboratories, Memphis. Composition: Essentially volatile oils including menthol, camphor and wintergreen, and a small amount of turpentine, in a mutton-fat base. Fraudulently represented as a treatment for influenza, sore throat, burns, etc.—[*N. J. 28743; November 1938.*]

Hayssen's (Dr.) Supreme Goitre Ointment.—H. H. Hayssen Co., and Hayssen Laboratories, Mobile, Ala. Composition: Potassium iodide (8.5 per cent) and small amounts of turpentine and rose perfume, in a petrolatum base. Fraudulent therapeutic claims.—[*N. J. 28744; November 1938.*]

Hayssen's (Dr.) Supreme Goitre Tablets.—H. H. Hayssen Co., and Hayssen Laboratories, Mobile, Ala. Composition: In each tablet, 0.163 grain of potassium iodide with inert ingredients such as sugar, starch and talc. Fraudulently represented as a remedy for goiter, tonsillitis, tumors, blood and nerve disorders, etc.—[*N. J. 28744; November 1938.*]

Liberty Blood Tonic.—National Medicine Co., Nashville, Tenn. Composition: Essentially extracts of plant drugs including a laxative and an alkaloid-bearing drug, compounds of iron, sodium benzoate, alcohol (7.2 per cent by volume), sugar and water. Fraudulent therapeutic claims.—[*N. J. 28988; November 1938.*]

National Kidney Preparation.—National Medicine Co., Nashville, Tenn. Composition: Essentially extracts of plant drugs, potassium acetate, sodium benzoate, alcohol (8.13 per cent by volume), sugar and water. For backache, bearing-down pains, lumbago, kidney and bladder troubles. Fraudulent therapeutic claims.—[*N. J. 28988; November 1938.*]

Pancreatone Capsules.—Crescent-Kelvan Co., Philadelphia. Composition: Glandular material and compounds of manganese, strychnine, arsenic and gentian. Fraudulently represented as a cure for diabetes and diseases generally of pancreatic origin.—[*N. J. 28742; November 1938.*]

Correspondence

THE BIOLOGIC ASSAY OF MIXTURE OF ACTIVE PRINCIPLES

To the Editor:—Expositions of the principles of biologic assay such as those by Dale and by Burn have done much in recent years to diffuse an understanding of the logical basis of the method. The principles seem so simple and so obvious that one may easily come to observe them in a literal, perfunctory manner without realizing how easily this may lead to fallacy.

Especially in the cases in which the drug to be assayed consists of a mixture of active components does it seem that a clarification of the principles is desirable. In this category, unfortunately, are some of the drugs for which biologic standardization is most essential. Digitalis, being one of the most important and most troublesome, will be considered in some detail.

That the drug must be compared with a standard which contains the same active principle is now generally realized; yet the difficulty of finding such a standard is not readily apparent. Objection was quite justifiably made to the use of ouabain as a standard for the assay of digitalis; but merely because a standard has now been adopted which has the name digitalis, one must not fall into the complacent assumption that all the logical requirements have been met.

A biologic assay is usually performed to determine therapeutic effectiveness in man, and the result is expressed in the form of a ratio which purports to represent the therapeutic activity of the tested preparation relative to a standard. If the drug assayed consists of a mixture of principles having qualitatively similar actions, to ascribe any such significance to this ratio involves one of the following assumptions: Either (1) all samples of the crude drug (including the standard) contain the several active principles in the same proportions or (2) the ratio of the dose producing the therapeutic action in man to the dose producing the observed action in the test animal is the same for each of the several principles.

The first assumption will be conceded to be not generally true. The fallacy involved in the alternative assumption is not so obvious. It is this proposition, probably, which is tacitly accepted in some standard procedures. The fact that the various antirachitic substances differ among themselves in their effectiveness in chickens relative to that in rats and the fact that one of the digitalis glucosides, gitalin, is reported to be three times as active therapeutically as was to have been expected from the biologic assay should constitute sufficient warning that any such assumption is unworthy of a priori acceptance.

Certain aspects of the therapeutic use of the cardiac glucosides add further confusion to the consideration. The glucosides differ greatly among themselves in the persistence of their action. A dose of a short acting glucoside and a dose of a long acting glucoside which are equivalent in the cat assay will obviously not be equivalent in maintaining digitalization in a patient. Moreover, the therapeutic effect itself, while imperfectly understood, undoubtedly is not one simple action. At least two effects, that on atrioventricular conduction and that on the efficiency of myocardial contraction, are involved in the usual therapeutic applications. It is not evident that the relative effectiveness in these two actions is the same for all the cardiac glucosides. If not, two glucoside preparations which are therapeutically equivalent for a patient with auricular fibrillation might not be equivalent for a patient with congestive failure without fibrillation.

These considerations force one to conclude that it is impossible to devise a scientifically sound biologic assay for a drug such as digitalis. The objection may be made that such cavilling is sterile pedantry—that the physiologic standardization of digitalis is a practical necessity, a practical success. It must be conceded that the usual assays of digitalis are sufficiently accurate for most clinical purposes. This is so because the two assumptions mentioned, while not true, are almost true. So far as either of these assumptions approaches the truth, the result of the assay approaches the therapeutic significance imputed to it. The assay will always be a compromise between logical integrity and the necessities of practical affairs and must be accepted with reservations.

Much work has been applied to the biologic assay of digitalis in the standardization of technic and in the mathematical analysis of animal responses. While it is laudable to try to eliminate all avoidable sources of error, much of this work must be considered a labor of futility. Furthermore, preoccupation with refinements has almost blinded some investigators to the fact that they are measuring something having no exact meaning in reality. However refined the technic, however refined the statistical treatment, the result cannot be more valid than the premises on which the method is based. There is need that more energy be devoted to the rigorous examination of the logical basis of biologic assays before it is profitable further to polish the technic of their performance.

THOMAS C. BUTLER, M.D., Nashville, Tenn.
Assistant Professor of Pharmacology,
Vanderbilt University School of Medicine.

INTRA-GROUP AGGLUTINATION

To the Editor:—In THE JOURNAL July 8, page 126, appeared an article by Levine and Stetson concerning a case of intra-group agglutination (immune iso-agglutination) after repeated transfusions. It makes no reference to my publication on the same subject in *Klinische Wochenschrift*, Nov. 14, 1936, page 1675. It must be emphasized that in the European literature there were five cases previous to mine in which sensitization was demonstrable of the red blood cells to blood of its own group. Only Deutsch's case resembled Levine and Stetson's; therein the symptoms of iso-immunization disappeared in a few weeks. In my case all samples of the B group blood cells showed agglutination without exception with the serum of the sensitive patient belonging to the B group, and none of the O group blood cells evidenced these symptoms. So it could be demonstrated by the indirect method that the immunization depends on the B factor and has nothing to do with the M, N and P factors. The direct method was not possible because the patient died a few days after the phenomenon of aplastic anemia appeared. The possibility, however, that the reaction becomes weaker and disappears in several weeks could therefore also not be excluded. But in spite of the short time that elapsed between the appearance of the symptoms and death, the determination of the titer of agglutination and the absorption of the anti-A agglutinins (normal agglutinins) was also possible. In view of the fact that the B group factor (agglutinogen) showed properties of antigen, its nature could be explained as albumin-like substance.

References:

Deutsch, B.: *Gyógyászat* 732 (Dec. 1) 1935.
György, P., and Witebsky, E.: *München. med. Wchnschr.* **76**: 195 (Feb. 1) 1929.
Lindan: *Acta path. et microbiol. Scandinav.* **5**: 382, 1928.
Traum, E.: *Deutsche Ztschr. f. Chir.* **237**: 97, 1932.

LADISLAUS MOSONYI, M.D., Baglyasalja, Hungary.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ACUTE LYMPHATIC LEUKEMIA

To the Editor:—**A 10 year old girl became ill June 1 with pain in the right shoulder. On June 15, pain and swelling of the left ankle with low grade fever set in. She was sent to the hospital June 26 with enlarged spleen and liver and palpable glands in the neck, axillas and groins. Several petechial spots were present; the temperature was 102 F. Blood study showed hemoglobin 48 per cent, red blood cells 3,040,000, white blood cells 2,150, polymorphonuclears 16 per cent, small leukocytes 50 per cent, large leukocytes 32 per cent, eosinophils 2 per cent and platelets greatly reduced; there was slight variation in size and shape of the red blood cells with moderate basophilic stippling; the reticulocyte count was 0.5 per cent; fragility test showed hemolysis complete in a 0.32 per cent solution and beginning in a 0.38 per cent solution; the sedimentation rate was 18 minutes; no growth occurred in blood culture. The Wassermann reaction was negative; x-ray study of the chest was negative. The diagnosis was acute aleukemic leukemia of the lymphocytic type. Treatment consisted of eight transfusions during the past seven weeks; ascorbic acid, liver extract and a high vitamin diet together with ultraviolet radiation from an air-cooled quartz mercury vapor arc lamp; roentgen irradiation of the spleen has been considered but not used. Four or five attacks of epistaxis occurred during the first month in the hospital and seemed to follow shortly after the transfusions were given. On July 3 the white cells had decreased to 750 with 7 per cent polymorphonuclears and 93 per cent small lymphocytes. On July 28 there were 11,000 white blood cells and apparently a remission of the symptoms. On August 4 there began a daily rise of temperature to 103 F. Two days later a sudden attack of severe upper abdominal pain with marked tenderness over the splenic area occurred. The tenderness disappeared in twenty-four hours. There has been gradual remission of symptoms until the present time, when the temperature in the afternoon is 101 F. The blood count August 16 showed hemoglobin 68 per cent, red blood cells 3,820,000, white blood cells 2,300, polymorphonuclears 36 per cent, small lymphocytes 62 per cent and large lymphocytes 2 per cent. The spleen has increased and decreased in size with the exacerbations and remissions of the disease, but the glands in the neck, axillas and inguinal region have remained as at first described—just palpable. Thank you for any assistance.**

M.D., Glen Cove, N. Y.

ANSWER.—This is apparently typical lymphatic leukemia of the acute or subacute type. No mention is made regarding the immaturity of the lymphocytes in the blood, but it is assumed that most of the large lymphocytes are lymphoblasts. Although no really curative treatment is known for any type of leukemia, it is of value to distinguish between the acute and the chronic forms because of roentgen therapy. This is contraindicated in the acute and subacute forms but may be fairly effective for a time in chronic leukemia. The treatment being given in this case is all that can be done unless the chronic form develops, in which case roentgen treatment should be used.

PAINFUL STIMULI OF THE TEETH

To the Editor:—**Will you please explain the physiology or pathology involved in the production of pain in the contact of sweets with an open cavity in a tooth. Since direct contact does not seem to be an essential factor and because the reaction is so rapid, I should like to know whether the production of pain is chemical or physical in nature. Even though the problem seems at first glance simple, I have been unable to explain it satisfactorily to myself.**

M.D., New York.

ANSWER.—The exact mechanism for the production of pain from stimuli acting on the substance of the tooth is not clearly understood in all its details. Chemical and physical changes affecting first the tissue fluid within the dentin appears to stimulate the nerve endings of the nonmyelinated nerve fibers within the tooth. There is considerable controversy at the present time as to whether these nerve endings are limited to the arborization about the body of the odontoblasts, whether they extend with the odontoblastic fiber (Tomes fiber) in the dentinal tubules or whether, as some believe, they reach farther and are incorporated within the calcified substance of the dentin.

Recently investigators, holding to the latter contention, believe that the failure of others to recognize these endings within the dentin has been due to the particular histologic technics used in the preparation of the tissue for study.

Stimuli arising through changes in temperature, pressure, surface tension and hydrogen ion concentration may be transmitted through the tissue fluid and in turn the fibers of the odontoblasts and from the odontoblastic substance to the nerve endings which are in contact either with the nerve endings within the dentinal tubule or the body of the cell which lies at the pulpal extremity

of the dentinal tubule. The stimulus reaching the afferent nerve fiber in this way is transmitted by them as they penetrate into the substance of the pulp and receive the myelinated nerve sheath before they leave the apical foramen and join their respective nerve trunk.

The enamel overlying the dentin acts as an insulation, and for this reason it may be easier to elicit reaction from stimuli at the neck of the tooth where the enamel is thin. Similarly, when the enamel has been destroyed by dental caries or any other cause the tooth may become sensitive. Conversely, in slowly progressive caries the sclerosis of which occurs as a degenerative change in the dentin the sensitivity of the tooth often decreases because of the formation of a nonvital, densely calcified substance protecting the underlying vital dentin.

The following references together with their bibliographies may be of interest:

Wassermann, Frederick: The Innervation of Teeth, *J. A. Dent. A.* **26**: 1097 (July) 1939.

Brashear, A. D.: The Controversy Concerning the Innervation of the Teeth, *J. Dent. Research* **16**:50 (Feb.) 1937.

EAR DROPS FOR EARACHE

To the Editor:—**I should like to develop ear drops for dispensing. I have been using glycerite of phenol in 5 and 10 per cent solutions. Can you suggest a solution without the phenol that will not cost much more than the glycerite of phenol? I have these solutions made up in pints and dispense them in 2 drachm bottles.** **M.D., Hamilton, Ohio.**

ANSWER.—For the purpose for which it is intended—the relief of earache—there is no better medicament than glycerite of phenol in solutions of varying strengths. To remove the phenol would rob it of its efficacy. This does not mean that solutions of glycerite of phenol do not have their limitations, but these do not become evident until after forty-eight hours or so, when the disagreeable desquamation which hides the landmarks on the drum begin to appear. By this time, if the symptoms are no better, the medication should be discontinued and paracentesis done. Plain glycerin has been recommended, but it does not have the analgesic effects of solutions of glycerite of phenol, although it does not produce the desquamation of which the latter is guilty.

INSULIN REFRACTORY DIABETES

To the Editor:—**I have at present under my care a patient who is apparently insulin resistant. This woman, about 50 years of age, has had hyperglycemia for the past two years. She has been given as much as 130 units of insulin a day by her local physician without effect. She is now hospitalized and is receiving 240 units of insulin a day. This does not have the slightest effect on her blood or urinary sugar. I have tried her on regular insulin, solution of zinc insulin crystals and protamine zinc insulin. They are all equally ineffective. She does not exhibit any allergic reactions to insulin. Physically she is rather short and stout, with a fairly dry skin. She has cataracts in both eyes. The remainder of her physical examination is entirely negative. I would sincerely appreciate any advice that you could give me as to the management of this case.** **Leonard J. Schiff, M.D., Plattsburg, N. Y.**

ANSWER.—Ever since its introduction there have been from time to time reports of unusual cases in which there is a remarkable insensitiveness to insulin. With these patients amounts of insulin as great as 200 or more units a day have been necessary. However, rarely if ever has complete resistance to insulin been demonstrated. Usually if the amount of insulin is steadily increased a point is reached at which hyperglycemia and glycosuria are controlled and further increase in insulin dosage causes hypoglycemia with the usual symptoms. One patient under observation has required from 300 to 400 units of insulin a day for almost four years, and another patient is now taking from 300 to 400 units a day, having at one time required as much as 2,270 units in a single day.

With the patient referred to by the questioner, one would advise gradual, yet steady, increase in the amount of insulin with the thought that finally a dosage will be reached to which the hyperglycemia and glycosuria will respond. During the period in which the insulin dosage is being steadily increased, frequent determinations of the amount of sugar in blood and urine should be made to avoid possible hypoglycemia. With such a patient it is imperative to carry out all possible studies to discover a cause for the insensitiveness to insulin. In certain of the cases reported in the literature, hemochromatosis, disorders of the endocrine organs other than the pancreas and extensive infection as from tuberculosis have been demonstrated. Attempts should be made to rule out particularly any disease of the pituitary gland. The function of the liver should be established by appropriate tests.

PREVENTION OF IMPETIGO IN NURSERY

To the Editor:—**Is the following recognized as a standard routine hospital procedure to prevent impetigo? "After delivery cleanse baby with Mennen's oil if necessary. Then apply ammoniated mercury 2.5 per cent over entire baby. Remove ammoniated mercury in twelve hours with Mennen's oil. No water or oil bath to be given after ammoniated mercury has been removed, but cleanse face, folds, buttocks, hands with Mennen's oil as necessary. On sixth day apply ammoniated mercury 1.5 per cent and remove same in twelve hours with Mennen's oil. Apply iodine 3.5 per cent daily followed by alcohol 70 per cent until cord drops off. Wash breasts after delivery with tincture of green soap followed with alcohol. Apply lanolin to nipples and binder. All suspicious areas to be reported and baby isolated. Doctors to wear cap, gown, mask and hands scrubbed before entering nursery." Are there many hospitals which subject all newborn babies to this procedure? Does it lessen the incidence of impetigo? Is it harmful to the baby's skin and mother's breasts?** **M.D., Minnesota.**

ANSWER.—The routine hospital procedure to prevent impetigo in the newborn nursery infant, described by the inquirer, is a more vigorous procedure than is used by most hospitals at present. In various modifications it is recognized in some hospitals as a standard routine procedure to prevent impetigo. It undoubtedly lessens the incidence of impetigo, although other less involved methods have also prevented impetigo. Iodine used after ammoniated mercury may give rise to severe dermatitis.

Some hospitals have been successful in preventing or lessening the incidence of impetigo by modifying these methods as follows: Sterile olive or cottonseed oil is used to cleanse the baby after delivery. The infant is then given a sterile oil bath every day until the day of discharge from the nursery, when a soap and water bath is given. The 2.5 to 3 per cent ammoniated mercury is applied after the initial cleansing and again on the fifth or sixth day. Only alcohol is used on the cord. Great care is observed not to irritate or traumatize the infant's skin by too energetic rubbing and wiping.

The mother's breasts are washed with ordinary soap and water (but not followed by alcohol) the first thing in the morning. A clean towel is then laid over them. Nothing more is used on the breasts before or after nursing or the rest of the day unless they are sore or cracked, in which case special orders are issued to meet the indication. The mother should wash her hands thoroughly with soap and water before handling her breasts at nursing time. It is well for the doctor to wear sterile rubber gloves when handling the infant. Much more important than the use of antiseptic ointments, oils or solutions on the infant's skin and mother's breasts is the observation by the nurses and doctors of practically aseptic technic in routine handling of the infants. No one should be allowed in the nursery who has an infected cutaneous lesion nor should a baby be taken to the breast if the mother has any. Separate nursery utensils should be used for each baby.

Another technic that is being adopted by more and more newborn nurseries and has been successful in preventing impetigo is the initial cleansing with sterile oil of the excess vernix caseosa and blood from the face, scalp and skin folds, great care being taken not to irritate or traumatize the skin. The infant is then placed in the crib and no baths or inunctions of any kind are given until the day the infant leaves the nursery. The infant is removed from his crib only to be taken to his mother. Of course vomitus and stool are cleansed off with gentle wipings of oil.

MYELORADICULITIS

To the Editor:—**I have a rather interesting case of myeloradiculitis superimposed on arthritis. A woman aged 46 has had all the possible paralyses, including collapse of the right lung. She has gradually convalesced after being ill some nine months; at present there is weakness of the sphincters of the bladder as well as of the rectum. Her fingers have contracted or flexed. She suffers from low back pains. Will any kind of electrotherapy prove beneficial to her? Would any orthopedic operation be of importance relative to a return of function of the fingers? Does myeloradiculitis permanently disable the patient or will there be a slow but gradual recovery?** **M.D., Pennsylvania.**

ANSWER.—Myeloradiculitis is a nonspecific disease which may have many manifestations. Usually it is of sudden onset and clears up equally rapidly with little residue. Other cases show gradual improvement over a period of years but rarely is there complete cure. Physical therapy in the form of heat, massage and mild manipulation of the extremities is beneficial in hastening the recovery. Electrotherapy is usually unnecessary and of no benefit. Orthopedic procedures should not be carried out until maximal recovery has taken place, which often takes from two to three years.

CONGENITAL SYPHILIS

To the Editor:—A white woman aged 24, married but subsequently divorced, was first seen Aug. 1, 1938. Her father died of a ruptured aortic aneurysm. At five weeks of age the patient had a right hemiplegia which resulted in a spastic right hemiparesis. At 10 years of age and again at 16 there were attacks of interstitial keratitis, but the patient had never received specific treatment. An amenorrhea had been present for two months. Nausea and vomiting were the presenting complaints. Physical examination revealed sclerosis of the right ear drum with marked loss of hearing; right spastic hemiparesis; anisocoria with the right pupil smaller than the left; anterior synechia deforms contour of the left pupil; slight "ground-glass" appearance of both corneas, especially the right, and slight suprapubic, symmetrical swelling—pregnancy (intra-uterine) of 3 months. The Wassermann reaction of the blood was strongly positive. Antisyphilitic therapy was begun at once and the patient received a total of thirteen intravenous injections of mapharsen and ten doses of 1 cc. each of bismuth salicylate in oil given intramuscularly. In January 1939 the patient was delivered spontaneously of a healthy male infant with no stigmas of heredosyphilis. The patient has had a return of headaches, which had been relieved during the pregnancy and treatment. The question now arises as to what therapy for the heredosyphilis is needed or justifiable. The Wassermann reaction of the blood at present is positive.

M.D., Oklahoma.

ANSWER.—It is important to determine whether the patient's headaches are due to congenital syphilis or to some other cause and particularly important to decide whether this symptom or any part of the patient's clinical picture is due to active neurosyphilis. It is suggested that lateral and anteroposterior roentgenograms of the head be taken and that the spinal fluid be examined at once.

If the spinal fluid is negative, it may be assumed that the majority of the patient's present objective signs are the residuums of old lesions during infancy and adolescence. Under these circumstances and whether or not the patient has an old osteitis of the skull, further treatment is to be regarded as prophylactic rather than as curative. In this case it is desirable to carry on with routine standard antisyphilitic treatment with alternating courses of an arsenical and of bismuth for a total period of about eighteen months dating from the original treatment.

Since the patient had a hemiplegia at the age of 5 weeks, it may be confidently assumed that there was once, if there is not now, severe involvement of the cerebral blood vessel. The point that now needs determination is whether there is also parenchymal involvement with the possibility of beginning juvenile dementia paralytica. If the spinal fluid is strongly positive, it is desirable to manage the patient as if she actually or potentially had dementia paralytica, first with fever therapy, preferably by induced malaria, and subsequently with tryparsamide and bismuth, treatment being continued for a minimum period of from two to three years.

RESIDUAL THROMBOPHLEBITIC EDEMA

To the Editor:—About one week after he suffered an infected lacerated wound of the left index finger a patient had an infarction of the base of the right lung. Two weeks later his right lower extremity became swollen and painful and a tender mass was palpated along the course of the saphenous vein. It was thought that the pulmonary infarction and the thrombosis of the vein were due to septic emboli originating in the infected wound. After a stormy course in the hospital he was able to return home three months after the onset of his illness. The edema persisted in the right lower extremity from the knee to the ankle. Some slight edema also appeared in the left lower extremity, but this was not pronounced. Elastic stockings were applied and he was permitted to return to work. At present the edema is still manifest and shows no tendency to disappear. It has been suggested by commercial houses that the use of the mercury diuretics intravenously is indicated in such conditions. Will you please comment on the value of such products in the presence of obstruction to the circulation. Any other form of treatment that you can suggest will be appreciated.

M.D., New York.

ANSWER.—A septic pulmonary embolus from an infected finger is a rare occurrence; the thrombus in the lower extremity cannot be of embolic origin unless there is a patent foramen ovale between the right and the left side of the heart and then it would have to be in the arterial tree. It is more likely that during the course of infection a latent thrombophlebitis of the lower extremity developed which gave rise to a pulmonary infarct and later resulted in a manifest venous thrombosis, a not infrequent course of events.

Efforts to relieve the residual thrombophlebitic edema are most successful when begun before the onset of any fibrosis. When the edema is allowed to persist, the plasma filtering out of the blood vessels sets up a connective tissue reaction and some edema is apt to persist. At this late stage the following measures may relieve some of the swelling: restriction of fluid intake to 1,500 cc. (this includes the water content of food), and restriction of salt to 4 Gm. a day and potassium chloride from 3 to 5 Gm. a day. During the night the edematous limbs or the entire lower end of the bed can be elevated several inches. A glycerin-gelatin cast, applied from the toes to the knee, or if necessary even to the groin, may be applied every three weeks for several months and is more effective than the elastic stocking in relieving the edema.

Mercurial diuretics relieve edema in the early stages a few days after the onset of symptoms (THE JOURNAL, April 2, 1938, p. 1075). Several months later in the presence of induration their effect is slight and temporary. Procaine block of the lumbar sympathetic chain is also quite efficient in relieving pain and edema in the acute stage but is not likely to help months or years later.

TREATMENT OF BLADDER AFTER REMOVAL OF TUBERCULOUS KIDNEY

To the Editor:—A man aged 35 who had complained of pain in the right loin and frequent urination with "burning" sensation for the past two months was submitted to a right-sided nephrectomy. He had had Pott's disease (lumbar) as a child. Preoperative examination showed that the man was apparently well nourished and not acutely ill. The blood pressure was 140 systolic, 90 diastolic. The eyes, ears, nose and throat were essentially normal. The neck showed the scar of a thyroidectomy (performed eight years before for an exophthalmic goiter and from which he made an uneventful recovery). The heart and lungs were apparently normal. The abdomen showed no tender areas or masses. The liver, spleen and kidneys were not palpable. There was right-sided infracostal tenderness, slight but definite. The reflexes were normal. Examination of the urine showed several red blood cells per high power field and a few pus cells. Smears and guinea pig inoculation proved the presence of a right-sided tuberculous bacilluria. The left kidney showed no evidence of tubercle bacilli on repeated smears and guinea pig inoculations. Kidney function tests of both sides gave negative reactions. A flat abdominal plate showed a round area (apparently of caseation) about one-half inch in diameter at the lower pole of the right kidney. The second and third lumbar vertebrae were fused as the result of the old tuberculous lesion. There was no evidence here of any activity. The left kidney appeared normal by intravenous and retrograde pyelograms. Cystoscopy revealed three small areas of ulceration around the right ureteral orifice, apparently tuberculous in nature. X-ray films of the chest showed some fibrosis but no active lesion. Postoperative inspection of the removed right kidney showed a large tuberculous abscess (three-fourths inch in diameter) at its lower pole. The wound healed without any complications. It is the surgeon's opinion that this patient should have roentgen treatment for his bladder and injections of old tuberculin in gradually increasing doses. I would appreciate your opinion of this type of postoperative therapy. What are the chances of the ulcerations of the bladder clearing up without roentgen treatment? What are the dangers, if any, of giving old tuberculin? Do you believe old tuberculin is indicated here? What is the prognosis in this case?

M.D., New York.

ANSWER.—It is probably not necessary to use x-rays in the treatment of cases of this kind. Most of the bladders involved in this way heal without any treatment other than general measures. Local treatment was in vogue some time ago, and it sometimes kept the local symptoms going and made them worse, often increasing the pain.

There are cases presenting extensive tuberculosis of the bladder that demand treatment of one sort or another, but in these cases neither local treatment nor roentgen therapy is indicated. The use of old tuberculin in this case is probably not necessary. One should rely on plenty of rest, sunshine, nourishing food and good old fashioned cod liver oil.

ALBUMINURIA IN YOUTH

To the Editor:—A boy and a girl, both 16 years of age, unrelated, came to me for a general physical check-up. In both cases the usual routine examination revealed mild secondary anemia and marked albuminuria. The latter was determined by use of Purdy's heat test as described in the sixth edition of Todd and Sanford's Clinical Diagnosis by Laboratory Methods, page 136. Can you outline for me a procedure which I can follow in order to determine the seriousness of the condition, the prognosis and the advice which I must give these patients regarding their future activity in regard to exercise and their choice of their life's work. The boy wishes to study medicine. Would the strain of long years of study and internship and the demands of active practice be too much? The usual search for foci of infection and the more common causes for this condition revealed nothing. The past history in each case indicates that the probable origin was scarlet fever in early childhood.

Erwin Steinman, M.D., Washington, D. C.

ANSWER.—The significance of albuminuria in children as evidence of organic kidney disease must be qualified by consideration of the possibility that the proteinuria is of the harmless, though frequent, type known as juvenile or orthostatic albuminuria. This diagnosis is made by exclusion of the known organic causes of proteinuria, by the demonstration of normal renal function (concentration test, phenolsulfonphthalein test or urea clearance) and of normal urinary sediment with the exception of a few hyaline casts, and by the typical absence of protein in urine secreted during the night or while the patient is at rest

after several hours in the recumbent position. Sometimes unusual precautions must be taken to obtain protein-free urine, because even the slight activity of getting out of bed to urinate may produce proteinuria. The patient should therefore be instructed to void after going to bed at night and again before getting out of bed in the morning. Exercise, cold showers and perhaps emotional stimulation may be followed by proteinuria in some children. A lordotic posture associated with rapid growth is often a factor in juvenile proteinuria. It should be remembered, however, that all these influences may also aggravate an organic proteinuria. If after the usual diagnostic procedures there is still the slightest doubt as to the nature of the proteinuria, an intravenous pyelogram is indicated to rule out common developmental anomalies, hydronephrosis and other urologic abnormalities. At this point a urologic consultant can be useful.

The prognosis and treatment will depend on the diagnosis. If the proteinuria is of the harmless variety, the child should be considered as perfectly healthy and not restricted as to activity or diet. Nutrition should be improved if necessary and iron given to increase the hemoglobin. Correction of poor posture by simple exercises may be helpful.

There is no reason to anticipate any unusual difficulties if such a patient should enter the profession of medicine, provided he is in good general health and possesses the other qualifications of a prospective physician.

If some organic renal disease is finally diagnosed, prognosis and treatment will vary with the type of disease and the degree of functional impairment. No more definite statement can be made without further details regarding the diagnosis.

OXYGEN FOR MIGRAINE

***To the Editor:*—Will you please let me know the status of oxygen tanks and gas masks in the treatment of migraine?**

Solomon Goodman, M.D., Brooklyn.

ANSWER.—The field of oxygen therapy has been greatly increased as the result of the ability to administer oxygen U. S. P. in the inspired air economically, efficiently and comfortably. Preliminary reports have been made by Boothby, Lovelace and Bulbulian and by Alvarez. In the report by the latter, the beneficial effect of the inhalation of oxygen U. S. P. in the treatment of migraine was first published. Boothby, Lovelace and Mayo gave further details in their paper at the recent meeting of the American Medical Association at St. Louis.

Severe headaches of the migraine type probably arise from several different causes. Boothby, Lovelace and Mayo reported that they most frequently obtained a beneficial effect when the patients had a definite prodromal period of from one to three hours' duration, if the oxygen was given during this period. Often when the oxygen was thus administered the attack was entirely aborted. Thus, in order that the method will be practicable, the patient should, under instruction from his physician, have the apparatus installed in his home so that at the first warning of the onset of the attack the inhalation of oxygen can be started.

Definite beneficial effect was less frequently obtained if administration of oxygen was not started until after the headache had fully developed and had become intense. Some of the patients who did not obtain complete relief from oxygen alone found that oxygen combined with small doses of ergotamine tartrate (gynergen) or other drug therapy was more effective than medication alone and often permitted the use of smaller amounts of drugs.

Inhalation of oxygen U. S. P. cannot be expected to be beneficial in all cases, but it seems as though it will prove to have a definite place in the treatment of migraine, either alone or in combination with drug therapy.

HEMORRHAGE IN ANTERIOR CHAMBER OF EYE

***To the Editor:*—Two months after a cataract operation, complicated by a severe and slowly absorbing hemorrhage in the anterior chamber only, would aspiration of the aqueous be a meritorious procedure in order to expedite earlier visual acuity? Has such a postoperative procedure been utilized and if so by whom and with what results?**

C. B. Greear, M.D., Honaker, Va.

ANSWER.—Puncture of the anterior chamber and aspiration of the blood are of value only when the blood is still fluid. After two months the probability is that extensive coagulation has taken place and that simple puncture of the anterior chamber would be useless; the clot would have to be grasped with forceps and pulled out. Such postoperative procedure has been in use for more than half a century and is discussed at length by Elschnig in the section on surgery in the second edition of Graefe-Saemisch.

CHRONIC SUPPURATIVE MASTOIDITIS

***To the Editor:*—A patient who had left chronic mastoiditis was operated on about seven years ago for the first time. The ear continued to discharge thick pus. Two years ago another operation was performed, at which time the ossicles were removed from the ear and the mastoid was again cleaned out. Since the second operation the mastoid wound heals, especially during the summer, and only a few drops of pus is discharged through the auditory canal. During the winter months pus forms behind the mastoid scar, which later breaks down, and pus is discharged through the mastoid wound as well as through the auditory canal. Of what value would irrigations and compresses of urea solution be in such a condition? Where may I find references on the subject?**

M.D., Pennsylvania.

ANSWER.—With the information given, it is not easy to answer this query. If the patient had chronic mastoiditis at the time of the first operation it is not quite clear why the ossicles were not removed from the ear at the first operation, because this is part of the classic mastoid operation for chronic suppurative otitis media.

There are a number of possibilities to explain the recurrence of the discharge from the mastoid wound and from the external auditory canal. A small amount of mucoid secretion should not be considered as due to a failure of the operation if there are no other symptoms. The improvement of symptoms during the summertime with their exacerbation in the wintertime might mean that frequent head colds were reinfecting the eustachian tube, which was not completely closed at the time of the operation. There is also the possibility that there are some peritubal cells which become infected in the wintertime, but this is less likely. Finally, there may also be some cells in other portions of the petrosal pyramid which discharge from time to time, although this type of involvement would be apt to be more constant throughout the year. All of these could exist even if it is assumed that the second operation was technically complete. Compresses of urea solution would probably do little good. Irrigations with a urea solution could be tried empirically and might be effective. As a further aid in the diagnosis, one could make x-ray films of the petrosal portions of the temporal bone and even use iodized oil, which could possibly be made to enter cellular structures by filling the external auditory canal and then using compression by means of a Politzer bag.

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TRAUMATIC ARTHRITIS WITH CALCIFICATION

***To the Editor:*—A woman aged 30 bumped her right elbow against a wall early in January 1939 and thereafter noted a progressive periarticular swelling with pain, increased heat and redness and limitation of motion. Some six weeks to two months later the arm was up in fairly acute flexion, no extension being possible because of extreme pain, and the skin was tight and glistening because of the swelling. The temperature varied from 97 to 98.6 F. by mouth. The white blood count remained at about 10,000 and there was a slight hypochromic anemia. General symptoms such as anorexia, headache and nausea were present but not marked. The first week in April a fairly definite collection of fluid was palpated about the joint, most of it lying medially, and aspiration revealed it to be red bloodlike fluid containing clumps of fibrin. Culture was taken but no report has as yet been made. The next day the pocket of fluid was opened widely and a soft rubber drain was inserted. This resulted in some recovery of function and definite improvement with respect to general swelling and pain, even though not as much fluid was encountered as had been expected. At the present time the patient is feeling fairly well, is eating well and has but little pain. However, x-ray examination yesterday revealed an area of calcification in the soft tissue medial to the joint, about 3 inches by 3 inches, conforming to the size and position of the fluid pocket mentioned, and this is apparently growing larger. She is not able to extend the forearm as far as she could after the pocket was opened. What is the modus operandi of the pathologic changes here found and what further treatment would you advise? Does the fact that she is three months pregnant have any bearing on the case? Your explanation of the pathology involved and suggestions for treatment will be greatly appreciated. Incidentally, a search for foci of infection has been entirely negative and she had no upper respiratory or other infections previous to onset. She is the mother of two children and her Wassermann reaction is negative, although she admits that she has had two miscarriages during the last four years, both occurring at about the second month.**

Bernard J. Voss, M.D., Columbia, Utah.

ANSWER.—If trauma to the right elbow is followed by periarticular swelling and pain, as well as local inflammation, but a rise in temperature or leukocytosis is absent, the inference would be that injury to the soft tissues had taken place and fluid, possibly bloody fluid, had collected. Moreover, calcification may have taken place in the fluid with resultant stiffness and limitation of motion. The fact that an incision was made and bloody fluid drained forth, but that pus was not encountered, would

support this inference. It is best to wait until complete calfication has occurred before any surgical procedure, including excision, is carried out. Such treatment, before calcification has become complete, usually tends to aggravate the condition. As a rule, roentgenographic examination from four to six months after injury will reveal that the condition is well demarcated, and then excision can be performed. In some instances flexion deformity of the capsule may be present and occasionally capsulotomy is indicated. Pregnancy may have an effect on the condition, since it may influence the degree of calcification.

Application of moderate heat may relieve some of the local pain but massage in such a condition is inadvisable.

NOCTURNAL NECK PAIN

To the Editor:—**A patient has pain in the lower occipital area nightly. He states that this pain has been constant every night for the past five years. He is never troubled during the day or evening and retires at night perfectly normal, falls to sleep easily and remains so until about 4 a. m., when he awakens from a sound sleep with a sharp, piercing pain in the region of the junction of the vertebrae and the skull, and sometimes the pain involves the first three or four vertebrae. The pain has always been in this particular area. He is compelled to get out of bed, and after walking around and massaging this area for a period of from fifteen to twenty minutes all symptoms disappear and he remains comfortable until the ensuing night. He advises me that about five years ago he had an ordinary stiff neck on arising in the morning and went to a chiropractor for adjustment. He received one treatment with no beneficial results and felt that his stiff neck was worse. These pains have been recurring daily ever since. He is 58 years of age and is normally healthy. The Wassermann reaction of the blood is negative; the differential blood count is normal, the red blood and white blood counts are normal and urinalysis is negative. X-ray films of the skull and vertebrae in different views are all negative and neurologic tests are all negative. The man has been under my care for the past two years and various treatments have been tried with no results. If you have any suggestions as to what this may be or any treatment, I would be very much obliged.**

M.D., Wisconsin.

ANSWER.—The fact that the pain comes on during sleep suggests that it is due to relaxation of the muscles of the neck. This always suggests tumor of the spinal cord, although this may or may not be the correct diagnosis; at least this diagnosis should be checked by a Queckenstedt test or perhaps injection of iodized oil if the neurologic examination reveals nothing.

ETHYL CHLORIDE OR CHLOROFORM AS INDUCTION AGENTS FOR ETHER

To the Editor:—**During the last eight years of my experience in anesthesia I have administered more than 200 anesthetics. In most of them the anesthesia used has been ether with ethyl chloride as the induction agent. I have had no fatalities directly attributable to the anesthesia while the patient was in the operating room. On three or four occasions I have had to give artificial respiration during the induction stage with ethyl chloride. On at least two occasions I have had to give short artificial respiration during the second stage with chloroform. I have practiced in a small city in which there is only one hospital. The Sister in charge of the hospital condemned the use of ethyl chloride entirely. The use of ethyl chloride as an induction agent to anesthesia has never been condemned by the medical staff of this hospital. From my experience I have found ethyl chloride to be of a valuable induction agent and a much more rapid one than chloroform, when given carefully in small amounts. Still, the Sister of the hospital forbids me to use ethyl chloride as an induction agent. She advocates chloroform instead. I might add that gas machines are not available. Is ethyl chloride too dangerous to use as an induction agent when carefully given in small amounts? Do you condemn its use entirely?**

M.D., Indiana.

ANSWER.—In the majority of hospitals, those who are qualified to be members of the staff are usually considered responsible for the choice of drugs to be administered.

As ethyl chloride and chloroform are both halogen derivatives of alcohol and are characterized by similar pharmacologic hazards, the use of either as an induction agent for ether anesthesia must be based on the ability, experience and judgment of the anesthetist.

ORANGE JUICE AND BAKING SODA

To the Editor:—**Please discuss the rationale of mixing in a little soda with orange juice when given to infants. Is there any reason at all for doing this?**

M.D., Texas.

ANSWER.—Orange juice contains citric acid, but it is not necessary to neutralize this weak organic acid by adding sodium bicarbonate. Because of its mineral composition, orange juice, although acid in taste and in reaction, is alkaline in the body. Large amounts of orange juice tend to make the urine alkaline. It is unnecessary to add sodium bicarbonate to orange juice, although if the juice is sour a little sugar may be added.

Medical Examinations and Licensure

COMING EXAMINATIONS

SPECIAL BOARDS

Examinations of the Special Boards were published in THE JOURNAL, September 23, page 1247.

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 18-20. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA: Phoenix, Oct. 3-4. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Basic Science.* Little Rock, Oct. 23. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock. *Medical (Regular).* Little Rock, Nov. 9-10. Sec., Dr. D. L. Owens, Harrison. *Medical (Eclectic).* Little Rock, Nov. 9-10. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written examination.* Sacramento, Oct. 16-19. *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California). San Francisco, Nov. 15. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: *Endorsement.* Denver, Oct. 3. *Examination.* Denver, Oct. 4-6. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Oct. 14. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven. *Medical (Regular). Examination.* Hartford, Nov. 14-15. *Endorsement.* Hartford, Nov. 28. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Medical (Homeopathic).* Derby, Nov. 14-15. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination.* Dover, July 9-11. *Reciprocity.* Dover, July 16. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, Oct. 23-24. *Medical.* Washington, Nov. 13-14. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, Nov. 13-14. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, Oct. 10-11. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Oct. 9-12. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

IDAHO: Boise, Oct. 3-4. Dir., Bureau of Occupational License, Mr. H. B. Wattlesey, State Capitol Bldg. Boise.

ILLINOIS: Chicago, Oct. 17-19. Acting Superintendent of Registration, Department of Registration and Education, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 18-20. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, Oct. 10. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, State Department of Health, Capitol Bldg., Des Moines.

KANSAS: Topeka, Dec. 12-13. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: Louisville, Dec. 5-7. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Portland, Nov. 14-15 Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St. Portland.

MARYLAND: *Regular.* Baltimore, Dec. 12-15. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, Dec. 12-13. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 14-16. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: Lansing, Oct. 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, Oct. 3-4. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Oct. 17-19. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: Kansas City, Oct. 26-28. Sec., State Board of Health, Dr. Harry F. Parker, State Capitol Bldg., Jefferson City.

MONTANA: *Reciprocity.* Helena, Oct. 2. *Examination.* Helena, Oct. 3-4. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science.* Lincoln, Oct. 3-4. *Medical.* Lincoln, Nov. 24-25. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

NEVADA: *Written examination and reciprocity with oral examination.* Carson City, Nov. 6. Sec., Dr. John E. Worden, 311 W. Robinson St., Carson City.

NEW JERSEY: Trenton, Oct. 17-18. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 9-10. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NORTH CAROLINA: *Reciprocity and Endorsement.* Raleigh, Dec. 11. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 2-5. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: *Basic Science.* Oklahoma City, Nov. 6. Sec. of State, Hon. C. C. Childress, State Capitol, Oklahoma City. *Medical.* Oklahoma City, Dec. 13. Sec., Dr. James D. Osborn, Jr., Frederick.

OREGON: *Basic Science.* Portland, Oct. 28. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, January. Dir., Bureau of Professional Licensing, Dr. James A. Newpher, Department of Public Instruction, 358 Education Bldg., Harrisburg.

RHODE ISLAND: Providence, Oct. 5-6. Sec., Board of Examiners in Medicine, Dr. Robert M. Lord, 122 Waterman Ave., Providence.

SOUTH CAROLINA: Columbia, Nov. 14. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Pierre, Jan. 16-17. Dir., Medical Licensure, Dr. G. J. Van Heuvelen, State Board of Health, Pierre.

TEXAS: Austin, Nov. 20-22. Sec., Dr. T. J. Crowe, 918-19-20 Mercantile Bldg., Dallas.

UTAH: *Reciprocity and Endorsement.* Salt Lake City, Oct. 10. Dir., Department of Registration, Mr. G. V. Billings, 324 State Capitol Bldg., Salt Lake City.

VERMONT: Burlington, Feb. 13-15. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 13. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WEST VIRGINIA: Fairmont, Nov. 6-8. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: Madison, Jan. 9-11. Sec., Dr. Henry J. Gramling, 507 Mariner Tower, Milwaukee.

WYOMING: Cheyenne, Oct. 2. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

New York Endorsement Report

Mr. Herbert J. Hamilton, chief, Bureau of Professional Examinations, reports 165 physicians licensed by endorsement from February 15 through July 15, 1939. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists	(1935), (1938) N. B. M. Ex.	(1937)	California,
Stanford University School of Medicine		(1937)	California
University of California Medical School		(1936)	N. B. M. Ex.
Yale University School of Medicine	(1934), (1935), (1936), (1937, 2) N. B. M. Ex.	(1927)	Connecticut,
George Washington University School of Medicine	(1931) District of Columbia, (1933), (1937) Maryland	(1917),	
Georgetown University School of Medicine	(1932), (1937, 2), (1938) N. B. M. Ex.	(1937)	New Jersey,
Howard University College of Medicine		(1937)	Tennessee
Emory University School of Medicine		(1921)	Georgia
Loyola University School of Medicine		(1930)	California
Northwestern University Medical School	(1931) Illinois, (1931) Maryland	(1913),	
Rush Medical College		(1937)	California
School of Medicine of the Division of the Biological Sciences		(1935)	Texas, (1937), (1938) N. B. M. Ex.
Indiana University School of Medicine	(1935), (1936, 2) Indiana	(1932),	
State University of Iowa College of Medicine		(1934)	Iowa
University of Kansas School of Medicine		(1925)	Kansas
Louisville Medical College		(1906)	Mississippi
Johns Hopkins University School of Medicine	(1934) N. B. M. Ex., (1928), (1933), (1934), (1938) Maryland	(1909)	Oregon,
University of Maryland School of Medicine		(1907)	Connecticut
University of Maryland School of Medicine and College of Physicians and Surgeons	(1935), (1937, 2), (1938) Maryland	(1936)	New Jersey,
Boston University School of Medicine	(1935), (1937, 4) N. B. M. Ex.	(1934),	
Harvard Medical School	(1920), (1930), (1932), (1936,3) N. B. M. Ex.	(1934)	New Jersey,
Tufts College Medical School		(1936)	N. B. M. Ex.
Wayne University College of Medicine		(1937)	Ohio
University of Minnesota Medical School		(1934), (1939)	Minnesota
St. Louis University School of Medicine	(1937) N. B. M. Ex., (1936), (1938, 2) Tennessee	(1930)	Missouri,
Washington University School of Medicine		(1931)	N. B. M. Ex.
Creighton University School of Medicine	(1938) Maryland	(1937)	California,
University of Nebraska College of Medicine		(1936)	California
Albany Medical College		(1937	N. B. M. Ex.
Columbia University College of Physicians and Surgeons		(1929), (1934), (1936), (1937, 3)	N. B. M. Ex.
Long Island College of Medicine		(1936), (1937, 2)	N. B. M. Ex.
New York Medical College and Flower Hospital	(1937, 17) N. B. M. Ex.	(1936, 2),	
New York University College of Medicine	(1938) California, (1936, 2), (1937, 4) N. B. M. Ex.	(1937)	Alabama,
University of Buffalo School of Medicine		(1936)	N. B. M. Ex.
University of Rochester School of Medicine		(1934)	N. B. M. Ex.
Duke University School of Medicine		(1936, 2), (1937)	N. B. M. Ex.
Eclectic Medical College, Cincinnati		(1938)	Ohio
Ohio State University College of Medicine		(1937)	Ohio
University of Cincinnati College of Medicine		(1939)	Ohio
Hahnemann Medical College and Hospital of Philadelphia	(1938) Maryland	(1931) Penna., (1937) N. B. M. Ex.,	
Jefferson Medical College of Philadelphia	(1933), (1936) New Jersey	(1915), (1931)	Penna.,
Temple University School of Medicine		(1929)	Penna.
University of Pennsylvania School of Medicine	(1934) N. B. M. Ex.	(1928)	Penna.,
Meharry Medical College	(1935), (1937), (1938) Tennessee	(1933)	N. Carolina,
University of Tennessee College of Medicine		(1936), (1938)	Tennessee
Vanderbilt University School of Medicine		(1938)	Tennessee
Baylor University College of Medicine		(1937, 3), (1938)	Texas
University of Texas School of Medicine		(1937)	Texas
University of Vermont College of Medicine	(1937, 4) N. B. M. Ex.	(1932),	
Medical College of Virginia		(1938)	Virginia
University of Virginia Department of Medicine		(1935, 2)	Virginia
Marquette University School of Medicine		(1938)	N. B. M. Ex.
University of Toronto Faculty of Medicine		(1925)	Illinois
McGill University Faculty of Medicine		(1933)	Minnesota
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1921) Ohio, (1936)	New Jersey
Hamburgische Universität Medizinische Fakultät		(1936)	New Jersey
Universität Köln Medizinische Fakultät	(1925) New Jersey	(1920)	California,
Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia		(1922) Massachusetts, (1936)	Maryland
Regia Università di Napoli Facoltà di Medicina e Chirurgia		(1935, 3)	New Jersey
Universität Basel Medizinische Fakultät		(1935)	Maryland
Université de Genève Faculté de Médecine		(1936)	Maryland

Book Notices

Malaria in Panama. By James Stevens Simmons, B.S., M.D., Ph.D., Lieutenant Colonel, Medical Corps, U. S. Army, with the collaboration of George R. Callender, M.D., Lieutenant Colonel, Medical Corps, U. S. Army, Dalferes P. Curry, M.D., Major, Medical Reserve Corps, U. S. Army, Seymour C. Schwartz, B.S., M.D., Dr. P.H., Lieutenant Colonel, Medical Corps, U. S. Army, and Raymond Randall, D.V.M., Lieutenant Colonel, Veterinary Corps, U. S. Army. The American Journal of Hygiene Monographic Series, No. 13, January, 1939. Supported by the De Lamar Fund of The Johns Hopkins University. Cloth. Price, $1.10. Pp. 326, with 32 illustrations. Baltimore: Johns Hopkins Press, 1939.

It is particularly opportune in the field of public health and preventive medicine that a complete account of the history and present status of malaria and malarial control at Panama should be written and that members of the Medical Corps of the United States Army should write it. It was here that General William Crawford Gorgas and his associates demonstrated that a great engineering enterprise need not fail even in the fever-stricken tropics if adequately provided and skilfully administered sanitation and medical service were supplied. Army organization, a vision of the problems, and medical and sanitary skill mastered malaria on a gigantic scale. Though whipped, malaria is rarely, if at all, completely vanquished. In the tropics, at least, the fight goes on continuously and ground gained is quickly lost when economy cuts down resources. Lieut. Col. J. S. Simmons writes the history of malaria on the Isthmus of Panama (1501-1938), Major D. P. Curry and Lieutenant Colonel Simmons describe malaria in the Panama Canal Zone (1904-1938) and Lieutenant Colonels Simmons, G. R. Callender, S. C. Schwartz and Raymond Randall give an account of malaria in the military forces of the Panama Canal Zone (1911-1938). The rainfall, aquatic environment and primitive culture of the natives in Panama afford ideal conditions for anopheline mosquitoes and the maintenance of plasmodium infections in man. From the earliest records of Spanish occupation malaria has impeded progress. It defeated all efforts at the construction of the transisthmian canal until it was held at bay. Since 1904 the records of the Panama Canal show that the incidence of malaria has greatly decreased in the sanitated cities of Panama and Colon, but surveys for the detection of human carriers and the experience of the U. S. Army in the field reveal the persistence of a high prevalence of malaria elsewhere in the republic of Panama. The morbidity in the Canal Zone decreased from 821 per thousand in 1906 to 16 in 1916, and subsequently rates have varied between 11 and 31. The increased efficacy of medical service is indicated by the fact that the death rate from malaria decreased from 8.7 in 1906 to 0.16 in 1914 and since that date only eighteen employees have died of malaria.

The large reservoir of human malaria carriers existing among the Negro farmers in the Canal Zone has not been reduced by free medication offered to persons found on recurrent monthly examinations to be carriers, possibly because the treatment is not sufficiently effective. Destruction of breeding grounds of anopheline mosquitoes by permanent sanitation for from 1 to 3 miles around towns and posts in which employees of the canal organization live has not prevented anophelines capable of long flights from entering the sanitated area from outside breeding grounds.

The incidence of malaria among United States troops maintained in Panama since 1911 has varied. It was highest, 208 per thousand, in 1914. The mean annual rates from 1916 to 1926 and from 1927 to 1935 were 81.5 and 65.9 respectively. For 1936 and 1937 it was only 39.4 and 40.6. The incidence of malaria in troops in Panama has always been considerably higher than among similar troops stationed elsewhere. It has been more prevalent on the Atlantic than on the Pacific side. The highest hospital admission rates occur at posts nearest unsanitated areas, and the lowest at those near large sanitated regions. The incidence falls in the dry season and is highest in the first half of the rainy season. It is also higher among troops than among employees, because of greater exposure of the former. Spectacular outbreaks have occurred during field maneuvers. Carriers are detected in and around military posts, and infected anophelines are present even in buildings during a large part of the year. More effective therapeutic treatment is needed.

No less than thirteen species of anophelines live in Panama, of which at least eleven are actual or potential vectors of malaria. The general conclusion of the whole matter is that better prophylactic methods are needed for the protection of troops in the field and more effective and less expensive procedures for the prevention of malaria among the inhabitants of the American tropics.

Die Herzkrankheiten: Klinik, Röntgenbild und Elektrokardiogramm. Von Dr. med. Paul Uhlenbruck, a. o. Prof. an der Universität Köln/Rhein. Second edition. Paper. Price, 36 marks. Pp. 422, with 413 illustrations. Leipzig: Johann Ambrosius Barth, 1939.

As in the first edition, the author has maintained the excellent manner of presentation. The number of illustrations and pages have been increased by a third. The author has enlarged the section on roentgenkymography and has added data concerning this method in various parts of the book. A section on the theory of the electrocardiogram as recently presented by Schellong has been revised, and sections have been added on the use of the vectordiagram and on the heart in diabetes. The part dealing with the electrocardiogram in left and right axis deviation has been expanded. The section on diseases of the coronary artery has also been greatly expanded and has been separated from that on heart failure. An attempt has been made to outline the appearance of the chest leads in this condition. While this section is a great improvement over the last, several of the diagrams used, such as figures 21 and 22, are fallacious, and it would have been better to use original curves rather than line diagrams to show the electrocardiographic contour in coronary disease. In the case reports more electrocardiograms with chest leads would have been valuable. The addition of several tables summarizing the electrocardiographic appearance in various types of heart disease was a great improvement. A new section dealing with the therapy of heart disease has been added and in it are given detailed tables of diets. A section dealing with functional tests of the circulation has also been added, and this is extremely valuable since it has been a much neglected subject in textbooks heretofore. Otherwise the text has been left almost unaltered. The book can be highly recommended to physicians interested in heart disease in showing the field of usefulness of the x-ray and electrocardiographic methods of studying the heart. The expert will find it useful in obtaining the present point of view of the German school. The attempt to enlarge the clinical side of the text in this edition may turn out to be more of a disadvantage than an advantage.

The General Tissue and Humoral Response to an Avirulent Tubercle Bacillus Including Growth Characteristics of the Organism. By Sol Roy Rosenthal, M.D., Ph.D., Associate in Bacteriology and Public Health. Joint Contribution from the Tice Laboratories of the City of Chicago Municipal Tuberculosis Sanitarium and the College of Medicine of the University of Illinois. Illinois Medical and Dental Monographs, Vol. II, No. 2. Cloth. Price, $3. Pp. 184, with 80 illustrations. Urbana: University of Illinois Press, 1938.

This monograph, primarily on BCG (Bacillus Calmette-Guérin), was written to determine whether a general cellular reaction of the tissues and the blood to the tubercle bacillus exists and, if so, what component of the antigen is responsible for the reaction. To this end, both the irritant and the irritated were examined to determine their variabilities and reactions. Obviously the literature on tuberculosis has not been completely reviewed because of its extensiveness, but the author has chosen sufficient bibliography to make the subject matter authoritative.

In the introduction, the organism and host factors are evoked to display the reticulo-endothelial system as having an important place in immunity, being especially prominent in its counteraction to the tubercle bacillus. Other cellular systems may also be of great import in immunity, but microscopic alterations in them are not detectable. A cycle of reproduction is noted for BCG if conditions are suitable, with sprouting of granules and non-acid fast stages described in chapter II. On the basis of animal inoculation, dissociation of BCG in the sense of increased virulence did not occur. Changes in the structure of colonies did transpire, but they were more or less transitory and probably associated with an arrest or acceleration of growth of the organism. The addition of crude BCG phospholipins, egg lecithin, cholesterol or neutral fats to mediums on which BCG was grown caused variations in the structure of the colonies of the bacillus which reverted. No increase in virulence of BCG was noted. Intracardiac injection of BCG caused not only a specific reaction, with the formation of tubercles in various organs, but also a generalized histiocytic response. This generalized reticulo-endothelial response was ascribed to "submicroscopic" forms of the tubercle bacillus. The formation and regression of the tubercle were traced. The blood picture reflected the tissue response. The number of bacilli and the organs involved determined to a large extent the proliferative or exudative character of the nodule. In chapter VI a line of reasoning is begun which might raise serious objections from those who do not subscribe to the view of ultramicroscopic or submicroscopic filter passing forms of the tubercle bacilli. The author was able to recover viable bacilli from animals although the antecedent organs failed to demonstrate positive cultures. These results (readily open to criticism) suggested the presence of submicroscopic forms and were thought to account for the stimulation of the reticulo-endothelial system. The term "submicroscopic" is defined as "forms that may evade detection because of their similar staining properties to the tissues. It does not necessarily imply forms too small to be seen by the microscope, although such forms are included." Such a definition can only lead to future confusion of the problem and rather weakens than strengthens the stand for BCG. Future researches must be more exacting on this point. In chapter VII the submicroscopic form is again called on as a poor defense for oral administration of BCG. Finally, chapter IX contains a summary; suggestive evidence is presented to indicate that elements of the tubercle bacilli not discernible microscopically are present in the organs of animals inoculated intravenously, intradermally and orally with mature forms of the organism. These forms can be recovered only after serial inoculation into animals. It is believed that they may be responsible for the generalized response of the reticulo-endothelial system. Whether or not the elements of the tubercle bacillus referred to are merely their granular constituents or true "ultraviruses" is not known. The inconclusiveness of this part of the author's work suggests a continuance of the search for superior and more exact weapons to solve this phase of the problem. In no wise does it detract from the tremendous value of this monograph, which not only presents the author's personal studies on BCG but also gives valuable evidence of the validity of the contentions by the French school that BCG is a "virus fixe" in the general sense.

The monograph is well printed on an excellent grade of paper chosen to do justice to the many half tone illustrations. The style of presentation of material and its order is also pleasing, even though many detailed experiments are cited. Although a truly scientific monograph written for the specialist on tuberculosis, it can be recommended to any physician interested in medical progress and investigation. The University of Illinois and editorial committee are to be complimented for making this monograph available at an extremely modest sum. Its scientific and educational value warrant their confidence.

Sleep, Your Life's One Third. By Maurice Chideckel, M.D., With a foreword by Robert Victor Seliger, M.D., Visiting Psychiatrist Johns Hopkins Hospital. Cloth. Price, $2. Pp. 183. New York: Saravan House, Publishers, 1939.

In this book the author offers to laymen his divers views and experiences. The style is clear and the quotations from many poets are copious. Many and various are the topics discussed, for example "the first authentic occurrence of murder by a sleep walker"; somnolence, which the author states is bought on mostly by the patient himself and which unfortunately "in quite a number of cases is followed by the catastrophic disease known as narcolepsy"; the vividness of certain dreams, as illustrated by a woman who swore she had sex relations with an angel; the freudian view which the author outlines and accepts that "if the father is suffering from sleeplessness, the girl with father attachment is sure to be afflicted with the same trouble." It is difficult to say just how the author classifies the causes of insomnia, but they seem to include schizophrenia and other psychotic states; "organic wakefulness"

due, for instance, to cancer of the prostate; pain, dyspnea; advanced kidney disease; anemia; "psychic sleeplessness, the commonest of all," such as follows an emotional shock or fear and excitement; toxic sleeplessness, resulting from overuse of alcohol and tobacco, as well as from tea and coffee, and sleeplessness due to digestive disturbances. The author evidently believes that insomnia is due to "afflux of blood in the brain." Regarding the "conquest of insomnia," he offers divers suggestions, including the treatment of any underlying disease discovered. The method which he seems to recommend most for general use is "light self hypnosis," after the method of Diethelm. Since the early nineties, various methods of "light self hypnosis" have been employed from time to time in this country for the treatment of sleeplessness. They have never proved popular among physicians. Among the reasons for this unpopularity probably is the failure of the method to apply suitably to the average patient. Psychologists also commonly condemn methods of self suggestion, often under the view that the remedy is worse than the disease.

Herz- und Kreislauferkrankungen in ihren Beziehungen zum Nervensystem und zur Psyche: Eine Einführung für Nervenärzte und Internisten. Von Dr. med. H. D. von Witzleben, Chefarzt des Sanatoriums Kreischa bei Dresden. Boards. Price, 4.50 marks. Pp. 101. Leipzig: Georg Thieme, 1939.

It is typical of the times that attempts should be made to correlate fields in internal medicine with the realm of neuropsychiatry. This the author has attempted to do as far as disturbances of the heart and circulation are concerned. He presents the current teachings in Germany as represented by some of the leading internists and psychiatrists. For the reader interested in obtaining such information this booklet is of value. Unfortunately, little reference is made to the work done in other countries; one has the feeling that much of what the author has to say is citation of authority. The reviewer is left with the impression that the subject is rather superficially considered. The material is divided into the following headings: (1) innervation of blood vessels, (2) blood supply and nerve supply of the heart, (3) tonus of the heart, (4) theory of nerve action, (5) cerebral circulation, (6) high altitude and compression, (7) blood pressure regulators (moderator nerves), (8) cardiovascular epilepsy, (9) cardiac catastrophes, (10) effect of changes of the psyche on the circulation and (11) circulatory psychoses and (12) the "nervous heart." Larger print should have been used and a bibliography appended.

Appendicitis: A Statistical Study. By Matthew Young and W. T. Russell. Medical Research Council Special Report Series, No. 233. Paper. Price, 30 cents: 1s. Pp. 64. New York: British Library of Information; London: His Majesty's Stationery Office, 1939.

Much of the data in this statistical report were obtained from published sources; of the thirty-six tables presented, a little more than half are original, comprising general data from England and Wales and more detailed material from three large London hospitals. The aim of the study as quoted in the preface was to obtain information "as to the factors which may influence the mortality." While such factors are mentioned as the marital state (single women are more likely to die of appendicitis than married ones), one looks in vain for detailed data which may have a therapeutic application, e. g. material on the question of delayed operation in appendical peritonitis, which is uppermost in the minds of many physicians. The only suggestive data on this question are contained in the comparative mortality rates from the London, St. Thomas's and University College hospitals. The last named, where immediate operation was the rule, reported by far the lowest mortality. In the other two hospitals a certain percentage of the patients were apparently treated along the delayed lines. The statistics indicate that appendicitis is on the increase in England and Wales, although the most conclusive data are contained in one table of figures from Scotland, where the incidence increased 23 per cent between 1930 and 1935 while sickness from other causes during this period remained the same. The reader would have more confidence in drawing inferences from these last figures if they applied only to acute appendicitis; a statement that they do cannot be found. Obviously, if chronic appendicitis is included, the value of statistical inferences is greatly weakened. Another point brought out in the report is the fact that the mortality rate in England and Wales has not increased in spite of the apparently increased incidence. Though the authors have not discussed this interesting and important feature in detail, one may dig out of table 18 a probable reason: fewer patients now enter the hospital with a ruptured appendix. In two London hospitals between 1900 and 1909, 1,772 cases of abscess and peritonitis were recorded, whereas between 1920 and 1929 but 1,264 such cases were listed, in spite of the fact that the total number of cases was nearly double in the later decade.

Recent Advances in Obstetrics and Gynecology. By Aleck W. Bourne, M.A., M.B., B.Ch., Obstetric Surgeon to St. Mary's Hospital, London, and Leslie H. Williams, M.D., M.S., F.R.C.S., Senior Obstetric Surgeon to Out-Patients, St. Mary's Hospital, London. Fourth edition. Cloth. Price, $5. Pp. 366, with 98 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1939.

An interval of seven years has elapsed between the appearance of the third edition and the present one. In this book the authors have included information concerning practically all the important advances made in obstetrics and gynecology during the past few years. In the section on obstetrics the subjects discussed are antepartum care, antepartum hemorrhage, breech deliveries, pyelitis, cesarean section, anesthesia and analgesia and puerperal sepsis. It is gratifying to see that antepartum care is receiving the important consideration which it deserves. Likewise cesarean section, particularly when combined with blood transfusion for the treatment of placenta praevia, is accorded an important place. In the treatment of pyelitis, mandelic acid and sulfanilamide are included. The authors are not convinced of the superiority of the cervical cesarean section over the classic one, but the only cesarean section they illustrate is the cervical one with a transverse incision in the lower uterine segment. The chapter on analgesia and anesthesia includes a discussion of practically all present day analgesics and anesthetics. In the treatment of puerperal sepsis, sulfanilamide is of course given special consideration. In the section on gynecology the subjects discussed are cancer of the uterus, sterility, prolapse, leukorrhea, sympathectomy, the sex hormones, ovarian tumors, the use of x-rays and physical therapy. The authors describe the technic and results of operation and radiation therapy for cancer of the cervix in various parts of the world. For the correction of prolapse they illustrate the Manchester operation, which is rapidly gaining in popularity, the interposition operation and the Mayo-Ward vaginal hysterectomy. The chapter on the sex hormones is brief and to the point. The chapters on ovarian tumors, the use of x-rays and physical therapy were written by Wilfred Shaw, H. Courtney Gage and Justina Wilson respectively. At the end of the book are special chapters on the Kielland forceps and the active principles of ergot. The book is well written, and the authors are to be congratulated on the selection of the material which they consider advances in obstetrics and gynecology.

Physiology of the Uterus with Clinical Correlations. By Samuel R. M. Reynolds, M.A., Ph.D., Associate Professor of Physiology, Long Island College of Medicine, Brooklyn, N. Y. With forewords by George W. Corner, M.D., Professor of Anatomy, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., and Robert T. Frank, M.D., F.A.C.S., Consulting Gynecologist, Mount Sinai Hospital, New York. Cloth. Price, $7.50. Pp. 447, with 44 illustrations. New York & London: Paul B. Hoeber, Inc., 1939.

This monograph on the physiology of the uterus will be a welcome contribution to the many investigators and clinicians interested in the problems of reproduction. The work comprises a comprehensive summary of the literature in this field as well as an intelligent interpretation of the available data. The bibliography of 1,190 references arranged alphabetically should be a great aid to any one working in this field. The physiology of uterine motility in experimental animals as well as in the human being is thoroughly considered. Chapters are devoted to innervation of the uterus, its blood and lymph supply, its metabolism and its growth. The hormonic control of physiologic changes, motility and reproduction are described in separate chapters. The relationships of the uterus to bodily functions are considered. Lastly, a chapter is devoted to a clinical contribution on the various endo-

crine problems as related to the physiology and pathology of reproduction. The author's extensive experiences over a period of years in this special field make him qualified to evaluate the data presented. Many investigators, however, may not agree with some of his interpretations and conclusions. The clinical observations are perhaps on less secure ground than the experimental. In spite of the large number of references in the bibliography, some excellent contributions have been omitted. The forewords of Corner, a renowned investigator in this field, and of Frank, a well known gynecologist, who has made many contributions in these special fields, attest the value of this contribution. The volume can be heartily recommended to all students interested in the problems of reproduction in any of its phases.

Recent Advances in Medicine: Clinical, Laboratory, Therapeutic. By G. E. Beaumont, M.A., D.M., F.R.C.P., Physician to the Middlesex Hospital, London, and E. C. Dodds, M.V.O., D.Sc., M.D., Courtauld Professor of Biochemistry in the University of London, London. Ninth edition. Cloth. Price, $5. Pp. 431, with 42 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1939.

This is an exceedingly valuable book. By no means all the matters treated are very recent, but this makes the volume more valuable because it serves to present each subject in a more thorough manner. Recent advances in biochemistry are well covered, and chemical procedures are briefly but adequately described. Advances in endocrinology are not so completely reported, but this is no doubt due to the fact that advances in this field have been so rapid that it is impossible to keep pace with them in a textbook. Recent contributions to our knowledge of virus diseases are neglected. On the other hand chemotherapy is well discussed, including the use of sulfanilamide and sulfapyridine.

Cancer: Causation, Prevention and Treatment. By A. E. Blackburn, M.D. Cloth. Price, 6s. Pp. 111, with 14 illustrations. London: H. K. Lewis & Co., Ltd., 1939.

In this treatise the author presents evidence which he believes establishes a relation between certain foods and cancer. He also emphasizes the effects of habits of modern civilization on the incidence of malignant disease. Certain clinical data are given, and a dietary treatment of cancer is suggested. Some interesting facts are noted concerning the incidence of cancer in different races. The author, who has traveled extensively, has made many personal observations in this respect. On the whole, the theories and conclusions, while interesting, will not withstand critical analysis and the student of this disease will ask for more convincing evidence before accepting the author's views on the cause and treatment of cancer.

Kurzgefasstes Lehrbuch der Psychiatrie. Von Professor Dr. Johannes Lange. Third edition by Dr. August Bostroem, Professor der Psychiatrie und Neurologie in Leipzig. Paper. Price, 7.20 marks. Pp. 276, with 4 illustrations. Leipzig: Georg Thieme, 1939.

Professor Lange, who recently died, leaves this edition of his brief textbook of psychiatry, which has been edited by Bostroem. It is a compendium which contains descriptive material of most of the usual psychiatric conditions in the orthodox kraepelinian fashion. Several works published in the United States are considerably better than this volume. In fact, its sterile descriptiveness without any dynamic or modern ideas tends to make it much less valuable than available American textbooks.

Beiträge zur psychiatrischen Erblehre auf Grund von Untersuchungen an einer Inselbevölkerung. Von Erik Strömgren. Acta Psychiatrica et Neurologica, Supplementum XIX. Denne Afhandling er af det lægevidensk-abelige Fakultet antaget til offentlig at forsvares for den medicinske Doktorgrad, København. Paper. Pp. 259. Copenhagen: Ejnar Munksgaard, 1938.

The author has studied the inheritance of psychiatric conditions in the Danish island of Bornholms, which he finds particularly suited for studies of an isolated group. He finds that the expectancy for schizophrenia is 0.65 ± 0.05 per cent and for manic-depressive insanity 0.36 ± 0.04 per cent. These figures are more or less typical of those published by other experimenters. There seems hardly any evidence to suggest that schizophrenia is not recessive and manic-depressive insanity dominant in their characteristic inheritance, according to the author of this statistical monograph.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Death of Diabetic Patient Following Withdrawal of Insulin by Drugless Healer; Manslaughter.—The defendant, Karsunky, was described in the record as a drugless healer but he had no license to practice in the state of Washington. He was charged in an information (1) of the crime of homicide growing out of the death of a diabetic patient resulting from the defendant's improper treatment and (2) of the misdemeanor of practicing medicine without a license. Having waived a trial by jury, he was found guilty by the court on both charges and appealed to the Supreme Court of Washington.

The patient, before he came under the defendant's treatment, was a strong, robust man, 33 years old, and engaged in heavy manual labor. For a period of three years he had had diabetes and had been a patient of Dr. Edgar Anderson, who prescribed a strict diet which regulated the intake of carbohydrates and required the patient to take every day about 15 units of insulin. By this treatment the patient was enabled to go about his work in the usual manner. The defendant, apparently an itinerant practitioner, stopped regularly at a certain hotel and prescribed for persons who called at his room. The medicines he prescribed were prepared by some company outside of the state and sold by the defendant in the original package to his patients. He used the title "doctor" in connection with his literature, labels and diet sheets and in making appointments with persons desirous of consulting him. On Dec. 11, 1937, the patient called on the defendant in the latter's hotel room and placed himself under his care. The defendant gave the patient no physical examination but did interrogate him. The patient informed the defendant of his diabetic condition and that he desired to discontinue the use of insulin. The defendant told the patient that he could cure diabetes, that his medicine would cure it but that his medicine and insulin would not mix. He advised the patient to discontinue the use of insulin and, in lieu of the strict diet prescribed by Dr. Anderson, the defendant gave the patient a new diet list which did not regulate the intake of carbohydrates. The defendant testified in the case that his reason for advising the patient not to take insulin was "because insulin is not human—it is not fit for any dog." That afernoon, the patient called on Dr. Anderson but did not advise him that he was under the care of the defendant. Dr. Anderson examined the patient and found he was in "grand condition" and "sugar free." On that date, the patient discontinued the use of insulin.

Two days later, the patient received by mail the medicines prescribed by the defendant and commenced to take them according to the directions sent with the medicines. On December 18, the patient was too ill to go to work and on the following day, December 19, he was confined to his bed and complained of feeling numb all over. On Monday, December 20, the patient's wife called in Dr. Anderson, who found the patient in a serious condition. He advised that the patient be placed in a hospital but the patient refused to go. That night, however, the patient was removed to a hospital and on his arrival was placed under an oxygen tent, given dextrose and saline solution with about 40 units of insulin. A blood sugar test was made but "the blood sugar report was so high that night that the physician could not get a reading." The next morning, the patient slipped into a comatose condition and during the day more insulin was administered to him. He died that evening. The autopsy disclosed that his death was due to diabetic coma.

The defendant contended that the evidence was not sufficient to sustain conviction on either count. But, the court pointed out, the practice of medicine includes the advice, whether oral or in the form of a written prescription, of a physician to his

patient as to what to do or what the patient should refrain from doing. Diagnosing, prescribing, orally or in writing, and treating ailments are constituent parts of practicing medicine. If one is so engaged, or holds himself out as being so engaged, he is guilty of violating the medical practice act if at the time of so doing he does not have a license authorizing him to practice medicine and surgery.

If the proximate cause of the patient's death, the court continued, was the advice and treatment given by the defendant, unless the patient's death was justifiable or excusable, the defendant is guilty of manslaughter. There was evidence that the medicines prescribed by the defendant were, under the medical practice act, drugs or medicinal preparations. The evidence was conclusive that the medicines prescribed and sent to the patient had little, if any, therapeutic value; their only effect on the patient was psychologic. The evidence was overwhelming, however, that the defendant's treatment of the patient's diabetic condition—giving him a diet list under which he was permitted to partake of unlimited quantities of carbohydrates and at the same time inducing the patient to discontinue the use of insulin—would inevitably cause the patient's death. The administration of such treatment by the defendant was through gross ignorance of the art he assumed to practice.

Five physicians testified that the only known and accepted treatment of diabetes mellitus is by the use of a restricted carbohydrate diet and the use of insulin, depending, of course, on the severity of the disease, and that to induce the patient to abstain from the use of insulin in view of "a case of his standing" would be the same as "signing his death warrant," as he absolutely could not live without taking insulin. There was no testimony, other than that of the defendant, contradicting the testimony of these physicians. When the defendant, the court continued, prescribed for the patient and attempted to treat him for the diabetes, without having a license to do so, he was engaged in an unlawful act. He was grossly negligent in furnishing a diet list that permitted the patient to eat unrestricted quantities of carbohydrates and at the same time advising and inducing the patient to dispense with the use of insulin. Prior to the time the defendant commenced to advise and treat the patient, the condition of the latter for three years under the treatment of a skilful physician had improved. The properly controlled carbohydrate diet and the use of insulin had resulted in the patient's being sugar free and permitted him to take care of his affairs in life just like any other man. The defendant assumed to treat the patient for diabetes mellitus, therefore he was bound to know the nature of the remedies he prescribed and also the treatment he adopted, and he is criminally responsible for the death resulting to the patient from gross ignorance in the application of the treatment.

The weight of authority is that criminal negligence exists where a physician or person assuming to act as such exhibits gross lack of competence. Criminal negligence may arise from failure to give proper instructions to the patient, or the giving, as in the present case, of improper instructions. To induce the patient to refrain from the use of insulin, which was necessary to preserve his life, is in principle the same as withholding the insulin from him by physical force. Whether by strength of mind or by physical power the defendant prevented the patient from using insulin, the principle is the same.

The defendant's counsel contended that the proximate cause of the patient's death was the failure of Dr. Anderson, when called to the patient's home December 20, properly to treat the patient who was then lapsing into a state of diabetic coma. But, the court said, there was no evidence from which a jury would be authorized reasonably to conclude that the patient's death resulted from anything that Dr. Anderson failed to do. Furthermore, if a person unlawfully inflicts on the person of another a wound calculated to endanger or destroy life, it would not be a defense to a charge of unlawful homicide, where death ensued, to show that the wounded person might have recovered if the wound had been more skilfully treated. Even unskilful or negligent treatment of the wound on the part of the wounded person or his physicians, which may have aggravated the wound and contributed to the death, does not relieve the assailant from liability. The court again emphasized the fact, however, that there was no showing that the treatment by Dr. Anderson on December 20 and 21 was the cause of the patient's death.

The court's attention was invited to a pamphlet, which was not offered in evidence, published by a manufacturer of insulin. Counsel for the defendant in his oral argument and in his brief quoted liberally from the pamphlet to support his theory that Dr. Anderson's failure "promptly to institute the precise treatment" needed when coma developed was the proximate cause of the patient's death. The rule is, the court said, that facts which are universally known, and which may be found in encyclopedias or dictionaries, are judicially noticed, provided they are of such universal notoriety and so generally understood that they may be regarded as forming part of the common knowledge of every person. The court refused, however, to take judicial notice of the facts in the pamphlet referred to. The pamphlet, standing alone, was not competent proof of the statements contained in it.

Under the law of Washington, a person charged with the commission of a crime may not waive trial by jury unless in his plea he admits the truth of the charge or in open court confesses his guilt. Not only is there an absence of statutory authority to waive trial by jury, but the right to waive, except in the two instances noted, is taken away. In the present case, the Supreme Court held that the defendant could not waive his right to a trial by jury and that because he was not given a trial by jury the judgment of the trial court must be reversed. The case was remanded with directions to the trial court to grant a new trial.—*State v. Karsunky (Wash.), 84 P. (2d) 390.*

Society Proceedings

COMING MEETINGS

American Academy of Ophthalmology and Oto-Laryngology, Chicago, Oct. 8-13. Dr. William P. Wherry, 107 South 17th St., Omaha, Executive Secretary.

American Academy of Pediatrics, Cincinnati, November 16-18. Dr. Clifford G. Grulee, 636 Church Street, Evanston, Ill., Secretary.

American Clinical and Climatological Association, Saranac Lake, N. Y., Oct. 9-11. Dr. Francis M. Rackemann, 263 Beacon St., Boston, Secretary.

American College of Surgeons, Philadelphia, Oct. 16-20. Dr. Frederic A. Besley, 40 East Erie St., Chicago, Secretary.

American Public Health Association, Pittsburgh, Oct. 17-20. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.

American Society of Anesthetists, New York, Oct. 12. Dr. Paul M. Wood, 745 Fifth Ave., New York, Secretary.

American Society of Tropical Medicine, Memphis, Tenn., Nov. 21-24. Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.

Association of American Medical Colleges, Cincinnati, Oct. 23-25. Dr. Fred C. Zapffe, 5 South Wabash Ave., Chicago, Secretary.

Central Association of Obstetricians and Gynecologists, Kansas City, Mo., Nov. 2-4. Dr. W. F. Mengert, University Hospitals, Iowa City, Secretary.

Central Society for Clinical Research, Chicago, Nov. 3-4. Dr. L. D. Thompson, 4932 Maryland Ave., St. Louis, Secretary.

Clinical Orthopaedic Society, Little Rock, Ark., and Oklahoma City, Oct. 13-14. Dr. H. Earle Conwell, 215 Medical Arts Bldg., Birmingham, Ala., Secretary.

Colorado State Medical Society, Colorado Springs, Oct. 4-7. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.

Delaware, Medical Society of, Wilmington, Oct. 9-11. Dr. John H. Mullin, 601 Delaware Ave., Wilmington, Secretary.

Gulf Coast Clinical Society, Mobile, Ala., Oct. 26-27. Dr. Clyde C. Rouse, 56 St. Joseph St., Mobile, Ala., Secretary.

Indiana State Medical Association, Fort Wayne, Oct. 10-12. Mr. Thomas A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

International Society of Medical Health Officers, Pittsburgh, October 16. Dr. Leon Banov, 12 Mill Street, Charleston, S. C., Secretary.

Inter-State Postgraduate Medical Association of North America, Chicago, Oct. 30-Nov. 3. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.

National Society for the Prevention of Blindness, New York, Oct. 26-28. Mr. Lewis H. Carris, 50 West 50th St., New York, General Director.

Pacific Coast Society of Obstetrics and Gynecology, Portland, Ore., Nov. 8-11. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.

Pennsylvania, Medical Society of the State of, Pittsburgh, Oct. 2-5. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Southern Medical Association, Memphis, Tenn., Nov. 21-24. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.

Tri-States Medical Society of Texas, Louisiana and Arkansas, Marshall, Texas, Nov. 8-9. Dr. Robert K. Womack, Longview, Texas, Secretary.

Vermont State Medical Society, Burlington, Oct. 5-6. Dr. Benjamin F. Cook, 154 Bellevue Ave., Rutland, Secretary.

Virginia, Medical Society of, Richmond, Oct. 3-5. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1929 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

9: 381-544 (July) 1939

Practice of Clinical Pathology in Relation to Medical Economics. T. B. Magath, Rochester, Minn.—p. 381.
Preparation of Anti-M and Anti-N Testing Fluids. I. Davidsohn and I. Rosenfeld, Chicago.—p. 397.
Toxicity and Therapeutic Effects of Sulfapyridine in Animals. M. W. Johannsen and A. V. St. George, New York.—p. 414.
Serum Proteins, Takata-Ara Reaction and Liver Function Tests in Lymphogranuloma Venereum. C. A. Jones and H. P. Rome, Philadelphia.—p. 421.
Incidence of Intestinal Parasites: Analysis of 2,265 Routine, Consecutive Stool Examinations in Outpatient Dispensaries of Charity Hospital of Louisiana at New Orleans. Emma S. Moss, New Orleans.—p. 437.
Laboratory Diagnosis of Infectious Mononucleosis. A. G. Foord and E. M. Butt, Los Angeles.—p. 448.
Xanthoproteic and Indican Studies on Blood in Renal Insufficiency. F. E. Kenny and R. S. Hubbard, Buffalo.—p. 465.
*Air Embolism as Complication of Artificial Pneumothorax. H. J. Schattenberg and J. Ziskind, New Orleans.—p. 477.
Uterine Lesions Associated with Fibromyoma. F. W. Light Jr., Springfield, Ill.—p. 483.
Examination of Cultures from Persons Suspected of Having Chronic Infection. G. H. Chapman, C. Berens, C. W. Lieb, W. B. Rawls, New York, and M. H. Stiles, Philadelphia.—p. 491.
Medicolegal Aspects of Chorionepithelioma in the Male. C. A. Hellwig, Wichita, Kan.—p. 504.
Specificity in Serodiagnosis of Syphilis: Differential Method: Preliminary Report. F. Rytz, Minneapolis.—p. 512.
Unusual Neoplasms of Small Intestines. S. A. Goldberg, Newark, N. J.—p. 516.

Air Embolism Complicating Artificial Pneumothorax.—Schattenberg and Ziskind believe it quite probable that air embolism as a complication following artificial pneumothorax is more frequent than is generally recognized. This may be due to the fact that, if a fatal termination does not occur, the condition is overlooked, called pleural shock or else this type of case is not reported in the literature. The infrequency of necropsies on patients dying from air embolism and the definite proof of the cause of death in the case that they report, the authors believe, warrants its recording. At necropsy air emboli were found in the left side of the heart, coronary arteries and cerebral vessels, and were observed clinically in the retinal vessels. No pneumothorax was found although five refills had been given. However, the amounts of these were small. The pleural cavity was entirely obliterated and one might assume that the air was administered into the air spaces within the lung. Barnwell states that this must be the case in many inductions. In the last and fatal insufflation the air was most likely administered intc one of the pulmonary veins, thus causing air embolism. The pressures found at the start of the refill tend to strengthen this conclusion. A diseased lung or pleura is necessary in the pathogenesis of this condition. When the lung is fibrotic and diseased, and this is the type of case in which air embolism usually occurs, the vessels are held stationary and are prevented from retracting or collapsing. Air introduced into a pulmonary vein or a blood vessel within adhesions, which establishes anastomoses with the pulmonary circuit, will travel to the left side of the heart and then into the general arterial circulation. There are three main theories as to the cause of death from air embolism. They are cerebral, respiratory with suffocation from the obstruction of the pulmonary artery, and cardiac the result of the lowering of intracardiac pressure and circulatory failure. The clinical symptoms will depend on that part of the body within which the air embolus lodges. In most cases giddiness, faintness, tickling of the throat, queer feelings or the coughing up of blood will be complained of. The patient may become pale or go into coma, and occasionally sudden death will occur. Splotching of the skin, transient blindness, diplopia, nystagmus, cyanosis, shock, profuse perspiration, chills, cardiac irregularity and respiratory failure may also be noted.

American J. Digestive Diseases, Huntington, Ind.

6: 361-428 (Aug.) 1939

Absorption of Hydrochloric Acid by Human Stomach. H. Shay, J. Gershon-Cohen and S. S. Fels, New York.—p. 361.
Treatment of Peptic Ulcer with Colloidal Aluminum Hydroxide. E. R. Kyger Jr., E. H. Hashinger and E. W. Wilhelmy, Kansas City, Kan.—p. 363.
Note on Value of Woldman's Phenolphthalein Test for Gastrointestinal Lesions. L. J. Notkin, E. Kirsch and S. Albert, Montreal.—p. 365.
Use of Secretin as Clinical Test of Pancreatic Function. J. S. Diamond, S. A. Siegel, M. B. Gall and S. Karlen, New York.—p. 366.
Surgical Treatment of Biliary Tract Disease: (*a*) Acute Cholecystitis. H. Koster and L. P. Kasman, Brooklyn.—p. 373.
Id.: (*b*) Chronic Lesions. H. Koster and L. P. Kasman, Brooklyn.—p. 376.
*Primary Cancer of Gallbladder. H. R. Liebowitz, Brooklyn.—p. 381.
Clinical Study of New Synthetic Spasmolytic Drug: Diphenylacetyl-Diethylaminoethanol. E. Spier, F. Neuwelt and H. Necheles, Chicago.—p. 387.
Gastrointestinal Pathology in Dogs Following Administration of Acetylcholine and Pitressin. H. Necheles and W. Masur, Chicago.—p. 389.
Experimental Pancreatic Fistula: Simple and Satisfactory Method for Investigating External Function of Pancreas. J. M. McCaughan, St. Louis.—p. 392.

Primary Cancer of Gallbladder.—Liebowitz reports twenty-eight cases of primary carcinoma of the gallbladder. Twenty-three of the cases occurred in women. This confirms previous observations that, like gallbladder disease in general, carcinomatous involvement predominates in women. The average age of the patients was 64.1 years. That calculi may be concerned in the genesis of the growth is indicated, as stones occurred in 71.4 per cent of the cases reviewed. The fundus and neck of the viscus are the most frequent sites of origin. Pathologically, the series consisted of fifteen scirrhous, eight papillary and three colloid adenocarcinomas and two epidermoid carcinomas. In one of the latter, typical prickle cells and nests of epithelial pearls were present. Carcinoma of the gallbladder spreads principally by contiguity, by the lymphatics, by way of the blood stream and also by way of peritoneal transplantation. The liver is most frequently implicated by secondary growths. Despite the rarity of skeletal involvement, metastases occurred to a lumbar vertebra. Splenic metastasis was observed once. Pain was the most frequent and constant symptom and was present in 67 per cent (nineteen) of the cases, in seventeen of which calculi were associated. A mass was noted in 60 per cent of cases and jaundice of the obstructive type in 46 per cent. Rapid weight loss was a significant observation. The cases have been characterized by a high incidence of surgical complications. Operative results have been ominous; in only one of sixteen surgical cases was there a possibility of cure. Carcinoma of the gallbladder is an insidious disease, eludes early diagnosis and is usually recognized in its later stages, when surgical extirpation is not feasible. Prophylactic removal of gallbladders containing calculi has been advocated.

American Journal of Medical Jurisprudence, Boston

2: 243-300 (July) 1939

Critical Review of the Medical Examiner System. B. M. Vance, New York.—p. 243.
Dying Declarations. E. O'Dunne, Baltimore.—p. 249.
Evidence of Intra-Uterine Death of Fetus. F. L. Adair and Edith L. Potter, Chicago.—p. 252.
Blood Alcohol. I. M. Rabinowitch and Betty Wilen, Montreal.—p. 261.
Fifty Years of Crime in America. J. E. Hoover, Washington, D. C.—p. 263.
Crime and Justice. S. Glueck, Boston.—p. 269.

American Journal of Ophthalmology, St. Louis

22: 833-952 (Aug.) 1939

Use of Sulfanilamide Compounds in Ophthalmology. J. S. Guyton, Baltimore.—p. 833.
Malignant Melanoma of Choroid: Further Studies on Prognosis by Histologic Type and Fiber Content. Helenor Campbell Wilder and G. R. Callender, Washington, D. C.—p. 851.
Lectures on Motor Anomalies: XII. Ocular Spasms. A. Bielschowsky, Hanover, N. H.—p. 856.
Intermittent Occlusion of Central Retinal Artery. T. E. Sanders, St. Louis.—p. 861.
Standards for Outpatient Service in Ophthalmology. C. Berens, New York.—p. 870.
Ophthalmic Surgery at Missions in India. S. G. Higgins, Milwaukee.—p. 876.
Perirrhaphy in Treatment of Corneal Ulcers and Opacities and of Interstitial Keratitis. E. Moretti, Catania, Italy.—p. 882.
Inhibitions of Autonomic Nervous System by Eye Stress. E. L. Jones, Cumberland, Md.—p. 887.
Oculoglandular Diseases, with Special Reference to Tularemia and Parinaud's Conjunctivitis. V. R. Hurst, Longview, Texas.—p. 891.

American Journal of Physiology, Baltimore

126: 417-802 (July) 1939. Partial Index

Coagulant Action of Crystalline Trypsin, Cephalin and Lung Extracts. J. H. Ferguson and B. N. Erickson, Ann Arbor, Mich.—p. 661.

Clotting of Hemophilic Plasma by Thromboplastic Enzyme. J. H. Ferguson, Ann Arbor, Mich.—p. 669.

Effect of Epinephrine on Blood Potassium. G. Brewer, P. S. Larson and A. R. Schroeder, Washington, D. C.—p. 708.

Electrocardiographic Changes and Concentration of Magnesium in Serum Following Intravenous Injection of Magnesium Salts. P. K. Smith, A. W. Winkler and H. E. Hoff, New Haven, Conn.—p. 720.

Sensitization of Motoneurons by Partial "Denervation." W. B. Cannon and H. Haimovici, Boston.—p. 731.

Measurement of Stroke Volume of Human Heart from Roentgenograms: Simultaneous Roentgenkymographic and Acetylene Rebreathing Experiments. A. Keys and H. L. Friedell, Minneapolis.—p. 741.

Influence of Adrenalectomy on Blood and Urine Ketones During Fasting and Anterior Pituitary Extract Administration. E. M. MacKay and A. N. Wick, La Jolla, Calif.—p. 753.

Annals of Medical History, New York

1: 315-404 (July) 1939.

Short Account of the History of Medicine in Lower Canada. H. S. Birkett, Montreal.—p. 315.

Early California Medical Journals. Frances Tomlinson Gardner, San Francisco.—p. 325.

Thomas Wade, Medical Student, 1851-1852. Mary Louise Marshall, New Orleans.—p. 343.

The Anatomic Compendium of Loys Vasse (1540). L. Crummer and J. B. deC. M. Saunders, San Francisco.—p. 351.

Molière and His Own Illness. L. Goldman, Cincinnati.—p. 370.

Aphorisms of Corvisart. A. L. McDonald, Duluth, Minn.—p. 374.

The Knee. D. W. Montgomery, San Francisco.—p. 388.

Medicine in the Life of Francois Rabelais. D. Slaughter, Dallas, Texas.—p. 396.

Annals of Surgery, Philadelphia

110: 161-320 (Aug.) 1939

Papilledema Without Intracranial Pressure (Optic Neuritis). W. E. Dandy, Baltimore.—p. 161.

Hurthle Cell Tumors of Thyroid. J. D. Martin Jr. and D. C. Elkin, Atlanta, Ga.—p. 169.

Retropharyngeal and Lateral Pharyngeal Abscesses: Anatomic and Clinical Study. M. Grodinsky, Omaha.—p. 177.

Primary Lymphosarcoma of Stomach. E. S. Taylor, New York.—p. 200.

Primary Closure of Peritoneum in Acute Appendicitis with Perforation: Report of Twenty Cases. R. Warren, Boston.—p. 222.

Congenital Cystic Kidney Treated by Ureteral Drainage. G. L. Hunner, Baltimore.—p. 231.

*Early Recognition of Shock and Its Differentiation from Hemorrhage. V. H. Moon, Philadelphia.—p. 260.

Dermoid Cysts of Vertebral Canal. E. B. Boldrey and A. R. Elvidge, Montreal.—p. 273.

Spinal Extradural Cyst Associated with Kyphosis Dorsalis Juvenilis. J. F. Robertson and C. P. Graham, Wilmington, N. C.—p. 285.

Postoperative Temperature Reactions: Reductions Obtained by Sterilizing Air with Bactericidal Radiant Energy: Seasonal Variations. D. Hart and S. E. Upchurch, Durham, N. C.—p. 291.

Differentiation of Shock from Hemorrhage.—Moon points out that the evidence from a review of the records of hemoconcentration or acute erythrocytosis indicates that hemoconcentration is related etiologically to the mechanism by which the syndrome of shock develops in various clinical conditions. Most of the authors attributed the hemoconcentration to the leakage of plasma through endothelium which had been rendered abnormally permeable by some injurious agent or condition. The author's experimental studies have included intraperitoneal introduction of muscle, liver and other tissue substances, injections of watery extracts of normal tissues, of bile and its salts, peptone, bacterial cultures and toxins, histamine, snake venoms and drugs such as emetine, barbital and the barbiturates. They also included burns, trauma, intestinal manipulation and obstructions, and the effects of proteins in sensitized animals. Regularly, and without exception, the agents and conditions mentioned produced hemoconcentration. This appeared early, and its degree was proportional to the apparent illness of the animal. When recovery followed, the blood returned to its normal composition. When death resulted, the postmortem observations were characteristic of shock. It appears that any agent or condition which affects capillary endothelium adversely will produce the syndrome of shock if that effect is produced systemically or in extensive visceral areas. Both the experimental and the clinical observations indicate that hemoconcentration is the surest and earliest clinical sign of endothelial damage of sufficient extent or degree to impair the efficiency of the circulation. It is strange that a phenomenon which is so grave in its import, so common in its occurrence and so easily demonstrated has not been utilized by physicians in their clinical studies of patients. Its use as a clinical test facilitates the early recognition and treatment of shock.

Archives of Ophthalmology, Chicago

22: 171-350 (Aug.) 1939

Mechanics of Prolapse of Iris in Cataract Operations: Clinical Observations and Method of Prevention. A. Hilding, Duluth, Minn.—p. 171.

Efficiency of Various Wound Closures in Prevention of Prolapse of Iris After Cataract Operations: Experimental Study. A. Hilding, Duluth, Minn.—p. 177.

Transplantation (Implantation) of Lacrimal Sac in Chronic Dacryocystitis. W. H. Stokes, Omaha.—p. 193.

Temperature Changes and Changes in Caliber of Retinal Blood Vessels After Short Wave Diathermy. I. Puntenney and S. L. Osborne, Chicago.—p. 211.

Instruments and Technics for Clinical Testing of Light Sense: II. Control of Fixation in Dark-Adapted Eye. Louise L. Sloan, Baltimore.—p. 228.

Id.: III. Apparatus for Studying Regional Differences in Light Sense. Louise L. Sloan, Baltimore.—p. 233.

Paradoxic Elevation of Lid. S. R. Gifford, Chicago.—p. 252.

Absorption Lines of Cornea. J. Laval, New York.—p. 257.

*Rickettsia Question in Trachoma: II. Louse as Possible Disseminating Agent for Virus. A. E. Braley, Iowa City.—p. 262.

*Familial Retinal Degeneration Leading to Detachment and Cataract Formation. B. Friedman, New York.—p. 271.

Cycloplegics. F. H. Thorne and H. S. Murphey, Washington, D. C.—p. 274.

History of Surgical Treatment of Retinal Separation. W. E. Krewson III, Philadelphia.—p. 292.

Louse and Trachoma Virus.—With the possibility in mind that trachoma is a rickettsial disease, it seemed likely to Braley that the louse should be considered as its vector, since trachomatous patients frequently are infested with these insects. He obtained head lice from patients with active trachoma. Approximately 8 per cent of lice are reported to harbor rickettsias in the gastrointestinal tract, but less than 1 per cent of the lice found by the author on American Indians contained rickettsias. A few smears showed extracellular collections of rickettsia-like bodies, but no intracellular collections were found. Mostly staphylococci were present in the smears. When ground lice were cultured on blood agar mediums only Staphylococcus albus grew. No bodies could be found that simulated the Halberstädter-Prowazek bodies or initial bodies of trachoma. Conjunctival epithelial smears of patients from whom the lice were obtained contained typical Halberstädter-Prowazek inclusion bodies. In none of the twenty eyes of baboons inoculated with ground lice from trachomatous patients did conjunctivitis develop. The material transferred from the conjunctiva of the same patients produced an active experimental trachoma in baboons. Six of the ten inoculated chick embryos died. Smears showed only staphylococci and degenerated cellular débris. Smears from the inoculated areas of the four embryos that lived showed young connective tissue cells, epithelium from the chorio-allantoic membrane and louse débris. No rickettsias were found. Sections of the chorio-allantoic membrane showed moderate hyperplasia of the epithelium at the site of inoculation but no evidence of rickettsias. Twenty lice were given intrarectal inoculation of known trachomatous material. In none of the five baboon eyes inoculated with these lice did conjunctivitis develop; however, the material used for injection produced experimental trachoma in a baboon.

Familial Retinal Degeneration, Detachment and Cataract.—Friedman observed over a period of several years a mother and seven children who presented a set of clinical manifestations which to his knowledge are unique in ophthalmology. These clinical data pertain first to the skeletal system and secondly to the eye proper. All the offspring except the oldest (female) bear a remarkable resemblance to the mother, who has the facies common to hyperpituitarism. All members of the family except the oldest child have myopic astigmatism. All the visible fundi are affected by a peculiar form of peripheral retinal degeneration, and in all but two of the children so affected there have occurred either complicating cataracts or retinal detachments or both. There is one exception: the oldest child has normal fundi. Examination of the fundi of these patients showed that the lesions were located in the extreme periphery. The lesions of the fundus began in the periphery and progressed slowly inward, but not far. The central two thirds

of the retina appeared free from pathologic changes. The vitreous in all cases in which it could be studied was degenerated and contained freely movable opaque strands. The family tree indicates the complications in the members of the series. A history of trauma to the eye or head antedated the detachments in three of the children. The violence of the injury was not severe, indicating the predisposition of such eyes to traumatic detachments of the retina. The author has no means of knowing how early in life the retinal lesions make their appearance, as all the patients were adults.

Archives of Otolaryngology, Chicago

30: 157-318 (Aug.) 1939

Neurologic Complications of Infections of Temporal Bone and Paranasal Sinuses: Summary of Twenty Years' (1919 to 1938) Experience. J. C. Yaskin, Philadelphia.—p. 157.
Origin and Distribution of Air Cells in Temporal Bone: Observations on Specimens from Twenty-Seven Infants and Sixty-Nine Human Fetuses. T. H. Bast and H. B. Forester, Madison, Wis.—p. 183.
Hypnosis: Potent Therapy for Certain Disorders of Voice and Speech. J. J. Levbarg, New York.—p. 206.
The Eustachian Tube: Abnormal Patency and Normal Physiologic State. H. B. Perlman, Chicago.—p. 212.
Rhinosporidiosis (Seeber): First Occurrence in a Female in North America. J. Ruchman, Brooklyn.—p. 239.
*Nasal Allergy in Children. E. J. Barnett and H. D. Carnahan, Spokane, Wash.—p. 247.
Otitic Sinus Thrombosis Causing Intracranial Hypertension. W. J. Gardner, Cleveland.—p. 253.
*Acute Infection of Circumvallate Papilla. R. Waldapfel, Grand Junction, Colo.—p. 269.
Tumors of Nose and Throat. G. B. New, Rochester, Minn.; W. Kirch, Des Moines, Iowa, and J. B. Erich, Rochester, Minn.—p. 283.

Nasal Allergy in Children.—In order to arrive at an accurate diagnosis and to obtain better results in the management and treatment of many nasal complaints in children, Barnett and Carnahan state that both the rhinologist and the pediatrician must become allergy conscious. To determine nasal allergy in childhood and to determine whether or not the allergy is complicated by infection, physicians need to perform routine examinations of the nasal secretions. Allergic control is vital if indicated surgical procedures are to be of benefit. Removal of infected tonsils and adenoids may aggravate symptoms in a child with uncontrolled allergy. Even though surgical intervention is indicated by x-ray or clinical observations, the results will be disappointing if associated allergy is not simultaneously or previously relieved. Removal of nasal polyps in the patient with uncontrolled allergy may be followed by prompt recurrence. Cytologic examinations of the nasal secretions with predominance of eosinophils offer confirmatory evidence of allergy. Local treatment for nasal allergy must be conservative. Prophylactic allergic measures are often sufficient to give relief from nasal allergy. Allergic testing and hyposensitization may be reserved for unrelieved or complicated conditions.

Acute Infection of Circumvallate Papilla.—According to Waldapfel, little is known about acute inflammations of the papillae of the tongue. These infections are usually included with diseases of the mucous membrane of the tongue and are not separated from the various types of glossitis. Such isolated infections occur and they offer diagnostic difficulties. The various papillae of the tongue offer a variety of conditions for the harboring of infectious organisms. He cites a case of infection of a circumvallate papilla, with retention and abscess formation, extreme pain on swallowing, intense pain of the tongue when touched, and coating of the tongue and the oral mucous membranes. Every severe process of this kind, the author points out, should be regarded as an isolated infection of a circumvallate papilla and its own related identical serous gland, which appears as a unit embryologically, anatomically and pathologically. The mode of infection is not known; perhaps injuries through foreign bodies in the food may play a part. The diagnostic difficulties arise mainly in the beginning of the disease and are due to the thick coating on the tongue and adjacent areas of mucous membrane, which covers the port of entry of the infection and the diseased area. This coating develops especially easily when the patient is not eating normally. Several points aid in making the differential diagnosis: Extreme tenderness of the tongue is manifest at the slightest touch without evident reason. The tongue is movable and apparently not greatly swollen, and the floor of the mouth is free from infection. The base of the tongue is free from involvement and there is no laryngeal edema present. The temperature is only moderately high. The prognosis is good. Heat (ultrashort wave diathermy) and antiphlogistic applications break down the papilla and spontaneous discharge results; if the condition is of long duration and fluctuation of the tongue is discernible, a superficial incision is advisable.

Canadian Public Health Journal, Toronto

30: 319-368 (July) 1939

Present Situation Regarding the Adequacy of Medical Care in the United States. N. Sinai, Ann Arbor, Mich.—p. 319.
Current Practice in Communicable Disease Control. H. Emerson, New York.—p. 325.
Value of Present Control Measures in Communicable Diseases. R. B. Jenkins, Ottawa, Ont.—p. 330.
Trial of Confidential Death Certificate in Providence of Quebec. P. Parrot.—p. 335.
The Cape Breton Island Health Unit. C. J. W. Beckwith.—p. 343.

30: 369-418 (Aug.) 1939

Prevention of Motor Traffic Accidents. A. H. Rowan, Toronto.—p. 377.
Survey of Control Measures in Highway Accidents in Canada. J. T. Phair.—p. 382.
Organization of a Public Health Nursing Service. Edna L. Moore, Toronto.—p. 387.
*Study of Goiter in Saskatoon, 1938. G. Binning, Saskatoon.—p. 393.
The Voluntary Health Agency. J. H. M. Jones.—p. 400.

Goiter in Saskatoon.—According to Binning, 166 cases of goiter (6.7 per cent) were found in 2,451 Saskatoon public school children. While age, sex, race and the social status were undoubtedly factors in the etiology, the source of water seemed to be the deciding factor. As adequate water analysis was not possible, some figures are presented showing that infected water (sterile or nonsterile), rather than the iodine content, was responsible for the occurrence of goiter. Severity seemed to be dependent to some extent on the source of water, those with slight goiters having a higher percentage of running water than those with moderate and large goiters.

Connecticut State Medical Society Journal, Hartford

3: 391-478 (Aug.) 1939

Diagnostic and Therapeutic Peroral Endoscopy. N. Canfield, New Haven.—p. 393.
Versatility of Cesarean Section. H. B. Perrins and M. Berlowe, New Haven.—p. 397.
Birth Control Issue in Waterbury. J. H. Foster, Waterbury.—p. 399.

Iowa State Medical Society Journal, Des Moines

29: 373-426 (Aug.) 1939

Radiation Control of Hyperparathyroidism. E. A. Merritt, Washington, D. C.—p. 373.
*The Jaundiced Bleeder: Control of Hemorrhage Through Vitamin K Therapy. H. P. Smith, S. E. Ziffren, C. A. Owen, G. R. Hoffman and J. E. Flynn, Iowa City.—p. 377.
Acute Pelvic Lesions in the Female, Diagnosis and Modern Management. C. W. Seibert, Waterloo.—p. 384.
Appendicitis: Mortality and Management. A. L. Jensen, Council Bluffs.—p. 390.
Study of Gordon Test for Hodgkin's Disease. L. H. Hoyt, Iowa City.—p. 394.
Nonspecific Foreign Protein in Ocular Therapeutics. S. D. Maiden, Council Bluffs.—p. 398.
Herpes Simplex of Cornea. C. A. Noé, Cedar Rapids.—p. 400.

Control of Bleeding Tendency in Jaundice.—During the last two years Smith and his colleagues observed about sixty cases of biliary tract disease, in most of which jaundice, together with a varying degree of prothrombin deficiency, was present. A number of these cases have been reported, and from the unreported group they cite four cases that illustrate a number of the problems which commonly arise. Evidence is reviewed to show that of patients with obstructive jaundice or biliary fistulas the bleeding tendency, so commonly observed, is due to faulty absorption of a fat-soluble vitamin, vitamin K. By suitable administration of this vitamin the bleeding tendency can be corrected, eliminating one cause of the high mortality in the surgical treatment of these patients. In order to determine the degree of vitamin K deficiency and to gage the dosage of vitamin to be administered it is necessary to know the plasma prothrombin level, for the determination of which the authors describe a simple bedside test. Purified preparations of vitamin K may be safely administered intravenously in cases in which nausea and vomiting preclude oral administration. The test to determine the plasma prothrombin level is carried out in a small serologic test tube of approximately 3 cc. capacity (75 by 10 mm.). Into the tube is placed 0.1 cc. of fluidextract of

thromboplastin. The tube is then filled up to the 1 cc. mark with freshly drawn blood. To obtain prompt mixing of the blood and thromboplastin the tube is inverted once over the finger and is then tilted gently every second or two in order that the beginning of clotting may be observed. In the case of normal blood, clotting occurs within twenty-five to thirty seconds; but, if the prothrombin level is low, the clotting time may be prolonged to several times this figure. By using normal blood as a standard control the patient's prothrombin activity may be expressed in terms of the normal standard. The following formula will be found suitable: Prothrombin activity (in percentage of normal) equals the clotting time of normal blood divided by the clotting time of the patient's blood multiplied by 100. The only technical feature in the entire procedure is the preparation of the thromboplastin solution. Fresh lung tissue (ox or rabbit) is cut into fine pieces and to each 10 Gm. of tissue 10 cc. of physiologic solution of sodium chloride is added. The mixture is stirred occasionally for the next two hours, after which it is strained through several layers of gauze. The pinkish opalescent fluid thus obtained is the thromboplastin used in the foregoing test. It keeps well for several weeks in the ice box or better still in the frozen state.

Johns Hopkins Hospital Bulletin, Baltimore

65: 145-222 (Aug.) 1939

Iron Metabolism in Infancy: I. Factors Influencing Iron Retention on Ordinary Diets. H. W. Josephs, Baltimore.—p. 145.
Id.: II. Retention and Utilization of Medicinal Iron. H. W. Josephs, Baltimore.—p. 167.
Relation of Syphilis to Nephritis. B. M. Baker Jr., Baltimore.—p. 196.
Inactivation of Testosterone Propionate and Estrone in Rats. G. R. Biskind and J. Mark, Baltimore.—p. 212.

Journal of Neurophysiology, Springfield, Ill.

2: 361-472 (Sept.) 1939

Axons as Samples of Nervous Tissue. H. S. Gasser, New York.—p. 361.
Initiation of Impulses in Axons. J. Erlanger, St. Louis.—p. 370.
Synaptic Mechanisms in Sympathetic Ganglions. D. W. Bronk, Philadelphia.—p. 380.
Transmission of Impulses Through Cranial Motor Nuclei. R. Lorente de Nó, New York.—p. 402.
Problems of Synaptic Function. A. Forbes, Boston.—p. 465.

Journal of Urology, Baltimore

42: 87-268 (Aug.) 1939

Right Solitary Renal Cyst: Left Renal Calculus. A. L. Greenberg, Brooklyn.—p. 87.
Metastasis in Hypernephroma. H. E. Kasten, Beloit, Wis.—p. 92.
Bladder Tumor Arising from Ovarian Dermoid Cyst: Case Report. J. M. Townsend, Birmingham, Ala.—p. 101.
Malakoplakia of Bladder: Case Report. D. F. Rudnick and A. B. Ragins, Chicago.—p. 108.
Adenocarcinoma of Bladder. S. R. Lowrey, Toronto.—p. 118.
Rhabdomyomyxosarcoma of Bladder: Case Report. V. Vermooten, Johannesburg, South Africa.—p. 126.
Upper Urinary Tract in Bladder Tumors. C. J. E. Kickham, Boston, and H. L. Jaffe, Wrentham, Mass.—p. 131.
Congenital Contracture of Vesical Neck. F. C. Hendrickson and K. Simon, Canton, Ohio.—p. 140.
Obstructing Prostate: Its Treatment, Surgical and Otherwise. G. G. Smith, Boston.—p. 145.
Leiomyomatous Prostate. M. R. Keen, Huntington, N. Y.—p. 158.
Hematogenous Hematuria. C. M. McKenna and C. La F. Birch, Chicago.—p. 171.
*Bacteriologic and Clinical Study of Bacillary Infections of Urogenital Tract. L. A. Sandholzer and W. W. Scott, Rochester, N. Y.—p. 183.
Intestinal Phase in Urologic Disease: General Considerations. R. Turell and A. W. M. Marino, Brooklyn.—p. 197.
Rectal Evipal Soluble Anesthesia in Urologic Procedures. O. Grant, R. Lich and J. Abajian, Louisville, Ky.—p. 204.
Simple Apparatus for Pneumo-Adrenalography. M. L. Brodny and H. A. Chamberlin, Boston.—p. 211.
Urography in Differential Diagnosis of Retroperitoneal Tumors. T. L. Schulte and J. L. Emmett, Rochester, Minn.—p. 215.

Bacillary Infections of Urogenital Tract.—Sandholzer and Scott made a study of the aerobic, gram-negative bacilli in 530 cultures recovered from 283 patients with infections of the genito-urinary tract. The aim of the investigation was to ascertain whether or not any relationship between the type of organism and the clinical course of the infection could be found. The bacteria fell into six genera. Members of Escherichia occurred in 83 per cent of the cultures (twenty-seven species or types) and members of Aerobacter in 13 per cent (fourteen species or types), while the remaining 4 per cent were distributed among the genera Proteus, Salmonella, Shigella and Pseudomonas. When specimens of urine from the same individual were cultured at intervals over a period of months, the type of organism recovered remained constant as to species and type of hemolysis, in some instances, but in other instances variations in either one or both of these factors occurred. Thus, from one patient nine different species belonging to three genera were recovered at various times. The author states that a larger series of cases than his will have to be studied before final statements concerning the reaction to therapy of individuals infected with the various types of bacteria are justified. However, his study does suggest that there may be a considerable variation in response to therapy. Thus, 66 per cent of the patients infected with Escherichia coli responded favorably to treatment. Of these, 78 per cent of the infections due to the beta hemolytic type and 80 per cent of those due to the gamma hemolytic type were cured, while only 66 per cent of the patients with nonhemolytic types responded well. On the other hand, only 38 per cent of the patients with infections due to Escherichia communior and 42 per cent of those infected with strains of Aerobacter were cured. Only 28 per cent of the patients with infections due to Proteus were cured.

Kentucky Medical Journal, Bowling Green

37: 317-376 (Aug.) 1939

Facial Paralysis: Recent Treatment with Case Report. A. L. Juers, Louisville.—p. 368.
Erythropoiesis. H. Gordon, Louisville.—p. 371.
*Staphylococcus Food Poisoning: Report of Outbreak. F. W. Caudill and E. C. Humphrey, Louisville.—p. 373.

Staphylococcus Food Poisoning.—Thirty-one cases of staphylococcus food poisoning are discussed by Caudill and Humphrey. On questioning the patients they found that one of two foods emanating from one establishment had been eaten by all of them: either hollandaise sauce or a cream sauce in which hollandaise sauce was used. Clinically the cases varied from fairly mild to extremely severe gastro-enteritis. In the severe cases there were persistent vomiting, cramps, profuse diarrhea and alarming prostration. One person had a blood tinged diarrhea and was so prostrated and dehydrated that intravenous sodium chloride and dextrose were thought necessary. In this case and in the others, the acute enteritis was over within eight hours and subsequent recovery was rapid and uneventful. Culture of a specimen of the hollandaise sauce revealed an almost pure culture of hemolytic staphylococcus, both aureus and albus. The cook stated that the sauce had been made about 8 o'clock in the morning and then used throughout the day. The cream sauce was served hot, illustrating the relative stability of the toxin to heat.

Mental Hygiene, Albany, N. Y.

23: 353-528 (July) 1939

Present Problems in Marriage Counseling. J. S. Plant, Newark, N. J.—p. 353.
Mental Disorder in CCC Camps. J. B. Dynes, Boston.—p. 363.
Art Technics for Use in Mental Hospitals and Correctional Institutions. F. J. Curran, New York.—p. 371.
Environmental Factors and Their Relation to Social Adjustment: Study of Group of Well Adjusted Children. D. A. Thom and Florence S. Johnston, Boston.—p. 379.
Organization of Ex-Patients of a Psychiatric Hospital. J. H. Friedman, New York.—p. 414.
Social Content of Work with Crippled Children. Esther M. Dimchevsky, Denver.—p. 421.
Plan for Training Psychiatrists. H. D. Coghill, Richmond, Va.—p. 432.
The Senile Sex Offender. J. M. Henninger, Pittsburgh.—p. 436.
Manners and Morals of Adjustment. A. A. Gross, New York.—p. 445.
Indications for Active Treatment in Childhood Difficulties. Beata T. Rank, Boston.—p. 456.

Military Surgeon, Washington, D. C.

85: 93-196 (Aug.) 1939

Age and Organic Efficiency. J. H. McCurdy and L. A. Larson.—p. 93.
Present Status of Anesthesia and Its Practical Application in Combat Zone. L. H. Mousel.—p. 103.
Diabetes Mellitus, with Particular Reference to Use of Protamine Zinc Insulin. O. B. Schreuder.—p. 113.
Addison's Disease: Consideration of Recent Advances in Treatment: Report of Case. M. C. Messina.—p. 122.
Débridement. M. R. Charlton.—p. 129.
Osteomyelitis of Jaw Bones. E. C. Fox.—p. 134.
Gum Rubber Base for Vulcanite Dentures. F. D. Knox.—p. 139.
Prosthesis in Case of Rhinoscleroma. E. Rothschild and D. Tanchester.—p. 142.
Experience in Treatment of Gas Bacillus Infection. M. J. Wilson.—p. 145.

Minnesota Medicine, St. Paul

22: 511-594 (Aug.) 1939

Diagnosis and Treatment of Low Back and Sciatic Pain Caused by Protruded Intervertebral Disk and Hypertrophied Ligaments. W. M. Craig and M. N. Walsh, Rochester.—p. 511.
Scattered Radiation and Variation of Roentgen Output of X-Ray Generators in Practice. W. Stenstrom and I. Vigness, Minneapolis.—p. 517.
Medical-Legal Aspects of Hospital and Medical Records. J. F. DuBois, St. Paul.—p. 520.
Fracture of Neck of Femur. F. S. Warren, Washington, D. C.—p. 523.
Acute Mesenteric Arterial Thrombosis. W. Ogden, St. Paul.—p. 525.
Confluent Calcification of Aortic and Mitral Valves. R. L. Nelson and A. H. Wells, Duluth.—p. 527.
Dermoid of Cerebral Hemispheres. R. C. Gray, Minneapolis.—p. 530.
Present Day Status of Juvenile Diabetes Mellitus: Review. J. M. Adams, Minneapolis.—p. 534.
*Aloes in Treatment of Burns and Scalds. J. E. Crewe, Rochester.—p. 538.

Aloes in Treatment of Burns and Scalds.—Crewe presents a method of treating burns and scalds which eliminates infection and waiting for the separation of the coagulum. He employs an ointment of which the active ingredient is socotrine, or Barbados aloes. The ointment is made by mixing 8 Gm. of the powdered aloes and about 8 Gm. of liquid petrolatum in an ounce (30 Gm.) of white petrolatum jelly. If liquid petrolatum is not used the ointment is a little too stiff. The usual preliminary precautions with regard to contamination and infection are taken. Blisters are carefully protected and the serum is evacuated with a hypodermic needle, after which enough mercurochrome is injected to cover the base of each collapsed vesicle. When this preliminary treatment has been completed, sterile gauze is folded in about four thicknesses to make an area large enough to cover the burn. The gauze is laid on a smooth, sterile towel and is covered with a layer of ointment at least one-eighth inch thick. This dressing is laid, ointment side down, on the burned area. More gauze may be placed on this dressing and the whole held in place with bandages or other material. No attempt should be made to spread the ointment on the burn, because it will not adhere readily to the raw surface. Ordinarily this dressing is not removed for two days. At the end of that time the entire dressing can be removed easily. There is no sticking from dried serum or dried blood. The surface of the wound does not bleed but has a clean, glazed appearance, as if the area were covered with a thin, transparent film. Unless new blisters have formed, another dressing, prepared as before, is applied and each dressing is left in place for two days. Usually, only from four to six dressings of aloes ointment will be required; after this zinc stearate or some other bland dressing may be applied. Cutaneous surfaces soiled by the ointment can be cleaned with benzine and the residue can be removed with rubbing alcohol. Aloes, used either as the leaf or the ointment, possesses distinct analgesic qualities. Dense, white scar tissue is not seen after healing of burns treated with aloes but the burned areas are reddish at first and remain smooth and pliable. Healing is rapid. Aloes possesses some enzymotic action; pus is apparently digested, for purulent surfaces become clean. The drug is astringent, possibly because of the tannin it contains. It has styptic properties in fresh cuts, when applied as a powder. Antiseptic properties are indicated by the rapid clearing up of infected surfaces. It might be feared that absorption would give rise to unpleasant effects, but none have been observed. Stools have not been loose in any case. No undesirable effect was seen when powdered aloes was dusted full strength, daily for a number of days, over the entire surface of large, chronic ulcers.

Missouri State Medical Assn. Journal, St. Louis

36: 317-352 (Aug.) 1939

Juxtadiaphragmatic Catastrophes: Three Unusual Cases. E. P. Heller, Kansas City.—p. 317.
Perforated Peptic Ulcer: Analysis of Thirty-Five Cases. V. W. Taylor, Bonne Terre.—p. 319.
Lymphogranuloma Venereum: Its Relation to Stricture of Rectum. W. G. Hook, Kansas City, and H. E. Bacon, Philadelphia.—p. 324.
Black Widow Spider Bite: Report of Two Cases. A. D. Vail, Springfield.—p. 330.
Heart Disease Complicated by Surgery. R. W. Maxwell, St. Louis.—p. 335.
Bilateral Aneurysms of Common Iliac Arteries. Jane Erganian and Bernice Albert, St. Louis.—p. 337.
Bromide Intoxication Involving Brain and Skin. A. L. Skoog, Kansas City.—p. 339.

Ohio State Medical Journal, Columbus

35: 807-914 (Aug.) 1939

Hematuria and Its Significance Following Automobile Accidents: Modern Means of Diagnosis and Treatment. L. P. Dolan, Toledo.—p. 825.
Hyperthyroidism: Relationship of Age of Patient to Manifestations of Disease. G. Crile Jr., Cleveland.—p. 828.
Diagnosis and Treatment of Left Subphrenic Abscess. B. N. Carter, Cincinnati.—p. 833.
Prevention and Treatment of General Peritonitis. B. Steinberg, Toledo.—p. 836.
Pneumococcic Meningitis. J. A. Toomey, Cleveland, and F. E. Roach, Rocky River.—p. 841.
Psychosis Due to Sulfanilamide. R. E. S. Young, Columbus.—p. 847.
Effect of Previously Performed Thyroid Operation on Involutional Psychosis. C. W. Sawyer, Marion.—p. 848.
"Port Wine" Mark (Naevus Flammeus) with Malignant Degeneration. I. L. Schonberg, Cleveland.—p. 850.
Benzedrine Inhalations in Asthma. M. Kalmon, Akron.—p. 851.
Activities and Program of State Department of Health. R. H. Markwith, Columbus.—p. 853.
Treatment of Acute Suppurative Peritonitis. F. T. Gallagher, Lakewood.—p. 855.
Graduate Surgical Training. C. A. Bowers, Cleveland.—p. 856.
The Management of the Asthmatic. M. B. Cohen, Cleveland.—p. 861.

Public Health Reports, Washington, D. C.

54: 1363-1422 (July 28) 1939

Anopheline Breeding: Suggested Classification of Ponds Based on Characteristic Desmids. W. C. Frohne.—p. 1363.
Factors Influencing Carcinogenesis with Methylcholanthrene: I. Effect of Age. M. B. Shimkin.—p. 1388.
Preparation and Cleaning of the NIH Anal Swab Used in Diagnosis of Oxyuriasis. J. P. Folan.—p. 1392.

54: 1423-1466 (Aug. 4) 1939

*Dermatitis Caused by a New Insecticide. L. Schwartz and L. H. Warren.—p. 1426.
Studies on Standardization of Gas Gangrene Antitoxin (Sordellii). Sarah E. Stewart and Ida A. Bengtson.—p. 1435.
Influence of Diet on Chronic Toxicity of Selenium. M. I. Smith.—p. 1441.

Dermatitis Caused by a New Insecticide.—Schwartz and Warren assert that while their report shows that alpha naphthyl isothiocyanate, base of a new insecticide, is a primary cutaneous irritant and a sensitizer, it is not recommended that its manufacture be permanently discontinued, because nearly all insecticides are cutaneous irritants or sensitizers, and when workers come in contact with new insecticidal preparations (as in this instance) dermatitis is likely to develop. It is the general experience that they can be safely manufactured under proper working conditions. However, before this new insecticide is placed on the market, actual experiments should be performed as to its effect on the skin of those who may be exposed to its action when it is sprayed, according to directions, in an enclosed room to destroy insects. Such tests can be made by spraying the insecticide containing alpha naphthyl isothiocyanate in a closed room in which a group of persons are exposed to its action for fifteen minutes a day for at least ten days and observed for ten days more. If one case of dermatitis should develop among 200 persons thus exposed, the product should not be placed on the market. If, as a result of such an experiment, it is decided to continue the manufacture of alpha naphthyl isothiocyanate, it is recommended that the manufacturing process be totally enclosed. Directions on cans of all insecticides should be worded in such a manner as to impress on the consumer the fact that the contents are toxic and irritating to the skin unless they are used according to directions. This would place the emphasis on their toxicity and tend to make people more careful in using them. The placing of poison labels on all insecticides would safeguard not only the health of the consumer but also the financial interests of the manufacturer by helping to protect him against law suits.

Rocky Mountain Medical Journal, Denver

36: 513-604 (Aug.) 1939

Abdominal Pain in Infancy and Childhood. J. W. Amesse, Denver.—p. 530.
Diverticulosis and Diverticulitis of Intestines. J. A. Bargen, Rochester, Minn.—p. 537.
Fibromyomas in Relation to Pregnancy, Labor and Puerperium. J. R. Wherritt, Salt Lake City.—p. 542.
*Surgical Treatment of Epilepsy. R. M. Stuck, Denver.—p. 547.
Socialized Hospitals, a Threat. H. A. Black, Pueblo, Colo.—p. 565.

Surgical Treatment of Epilepsy.—Stuck suggests that many chronic epileptic patients, when studied carefully, will be found to have definite operative cerebral lesions. These focal lesions, which are varied in nature, are so situated that they

are irritating to the cortex. In some cases the lesion is a contracting scar from an old compound skull fracture; in others it is a tumor, an abscess, an old encephalitis, meningitis, a hemorrhage or the like. In order to determine the character and location of the focal lesions, a carefully taken history, with special reference to the sequence of events in the attacks, as well as an encephalogram or ventriculogram, is essential. It may even be necessary for the physician to place the patient under observation in the hospital and to produce a few attacks in order that they may be accurately observed. Overfunction of the cerebral cortex usually results in an epileptic fit or convulsion. When there is a widespread disturbance such as a toxemia, the convulsion is generalized from the onset. Occasionally, however, the patient does not lose consciousness or have a generalized convulsion, although he may develop a generalized convulsion later. In such a case it not infrequently happens that the patient experiences an initial localized movement or sensation, known as an aura or hallucination, which is followed by a spread of this impulse over the body like a ripple across a pool of water, until the whole body is affected, consciousness is lost and a major convulsion ensues. The most valuable study of the seizure is made in the period before consciousness is lost. By intimate questioning at this time it is possible to identify the manner of onset of the attack and to localize grossly the cerebral focus. The initial event in the convulsion "signatures" the focus and is therefore the most important bit of information in the history. This "signature" may be manifest by a numbness, a tingling or a feeling of deadness of the finger, the hand or the foot; by a local weakness, a hallucination of smell, taste, odor or sight, as shown by flickering of lights, or by a temporary inability to speak.

South Carolina Medical Assn. Journal, Greenville

35: 193-216 (Aug.) 1939

Management of Some Problems of Thoracic Surgery. F. P. Coleman, Columbia.—p. 193.
Report of the Committee on Maternal Welfare. R. E. Seibels, Columbia.—p. 202.

Southern Medical Journal, Birmingham, Ala.

32: 793-890 (Aug.) 1939. Partial Index

*Antipellagric Action of Pyrazine-2, 3-Dicarboxylic Acid and Pyrazine Monocarboxylic Acid. C. E. Bills, F. G. McDonald, Evansville, Ind., and T. D. Spies, Cincinnati.—p. 793.
Some of the Experimental Lesions Produced by Staphylococcus Toxin. R. H. Rigdon, Nashville, Tenn.—p. 798.
Spinal and Epidural Analgesia in Gynecology and Obstetrics: Analysis of 8,233 Cases. P. Graffagnino, New Orleans.—p. 802.
*Clinical Use of New Synthetic Estrogenic Hormone, Stilbestrol: Preliminary Report. K. J. Karnaky, Houston, Texas.—p. 813.
Pregnancy and Cervix Cancer. Q. U. Newell and W. C. Scrivner, St. Louis.—p. 818.
Psychogenic Basis of Gastrointestinal Symptoms. L. Martin, Baltimore.—p. 825.
Convulsive States. H. R. Unsworth, New Orleans.—p. 831.
Misbehavior Patterns of Alimentary Tract: Clinical Study with Illustrative Cases. A. L. Levin, New Orleans.—p. 833.
Gastrointestinal Allergy, with Special Reference to Esophagus. O. R. Withers, Kansas City, Mo.—p. 838.
Malaria in Southern States. W. N. Bispham, Baltimore.—p. 848.
Malaria Prevention Activities, 1938. L. L. Williams Jr., Washington, D. C.—p. 851.
Recent Advances in Epidemiology of Malaria. R. B. Watson, Wilson Dam, Ala.; E. C. Faust, New Orleans, and J. S. Simmons, Boston.—p. 853.
Recent Advances in Entomologic Knowledge of Malaria Control: Report of the Subcommittee on Entomology. E. H. Hinman, Wilson Dam, Ala.—p. 857.
Pustular Perichondritis of Ears. C. F. Lehmann and J. L. Pipkin, San Antonio, Texas.—p. 874.

Antipellagric Action of Certain Acids.—Bills and his associates used either pyrazine-2, 3-dicarboxylic acid or pyrazine monocarboxylic acid in the treatment of the glossitis of twenty-three pellagrins. Within two to twelve hours after the administration of the acid, the patients reported a great increase in sense of well being and relief from glossitis. Rapid fading of the glossitis was evident on objective examination. Of the six patients for whom therapy was discontinued after the glossitis disappeared, who remained on their usual inadequate diets, the symptoms reappeared within two weeks in each instance. Each of these patients was treated as before and responded in an identical manner. In general, the clinical response following the oral administration of either acid is similar to that following the administration of adequate amounts of nicotinic acid. In contrast to nicotinic acid, these two pyrazine compounds do not produce the vasodilator symptoms which often follow the use of large doses of nicotinic acid. The maximal and minimal dosages for oral use have not been determined, but a total of from 500 to 800 mg. of either pyrazine-2, 3-dicarboxylic acid or pyrazine monocarboxylic acid, administered in divided doses from five to eight times a day, is safe and effective. The authors state that further studies are in progress to determine the therapeutic usefulness of these new agents in comparison with the established remedies for pellagra.

Clinical Use of Stilbestrol.—Karnaky believes that since the advent of diethyl stilbestrol it is no longer necessary to fight and wrestle with children who have a vaginal discharge or gonorrheal vulvovaginitis. Tablets of this estrogenic substance have a sweet taste and are pleasant to take orally. The child likes to take them because they are pink and resemble candy. It is no longer necessary to give injections or insert suppositories or give sulfanilamide, which is toxic to these children. The synthetic estrogenic diethyl stilbestrol can be used in all cases in which natural estrogen has been used. Functional uterine bleeding can be stopped more quickly by the injection of 5 mg. of diethyl stilbestrol than in the time required to take a patient to a hospital and to prepare her for and perform the dilation and curettage. The best tolerated and most effective dose is 0.1 mg. two or three times a day by mouth after meals or the whole dose at bedtime. Patients become tolerant to diethyl stilbestrol. In all the author states that he has treated, with this drug, twenty-five cases of amenorrhea, sixty of the menopause, sixteen of senile vaginitis, sixty of menometrorrhagia, eleven of hypomenorrhea, two of painful pelvis, five of vulvovaginitis, five normal women and five of complete abortion.

United States Naval Med. Bulletin, Washington, D. C.

37: 367-522 (July) 1939. Partial Index

Loss of Intermaxillary Distance: Effect on Aviators and Relief by Interdental Splint. R. A. Lowry.—p. 367.
Perception Time and Night Blindness. J. H. Korb.—p. 392.
Medical Care of Dependents on Naval Personnel. E. D. McMorries.—p. 415.
Hospitalization of Naval Dependents. J. R. White.—p. 444.
Seasickness: Etiology and Treatment. J. R. Poppen.—p. 463.
Id.: From a Patient's Point of View. W. S. Sargent.—p. 480.
Airsickness. C. C. Yanquell.—p. 486.
Use of Oxygen in Body Cavities, with Illustrative Cases. W. S. Bainbridge.—p. 489.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

47: 429-506 (Aug.) 1939

Conservative Treatment of Appendicitis. H. E. Mock, Chicago.—p. 429.
*Prognosis of Malignant Goiter in Relation to Pathologic Types. R. Ward, San Francisco.—p. 437.
Value of Blood Iodine Determination from Clinical Point of View. H. R. Litchfield, Brooklyn.—p. 449.
Hemorrhagic Diathesis in Patients with Jaundice: Relationship of Physiologic Mechanisms to Morbid Anatomic Changes. E. W. Boland, Los Angeles.—p. 459.
Complications, Predisposing Causes and Possible Routes of Spread of Infection in Extraperitoneal Cesarean Section. A. Bernstein, San Francisco.—p. 462.
Parotitis and Staphylococcus Aureus Septicemia as Surgical Complications. E. A. Pearson, Los Angeles.—p. 468.
Postoperative Intestinal Obstruction: Its Early Recognition and Management. E. S. Morgan and F. F. Henderson, Boston.—p. 474.
Symmetrical Cortical Necrosis of Kidneys: Report of Two Cases. C. P. Larson and R. J. Bennett, Fort Steilacoom, Wash.—p. 481.
Surgical Approach to Hypertension: Division VII. F. M. Findlay, San Diego, Calif.—p. 485.

Prognosis of Malignant Goiter.—Ward shows the relationship of prognosis to the microscopic picture in seventy-seven of eighty-four cases of malignant goiter in which pathologic studies are available. It was found that papillary carcinoma offers a better prognosis than any other form of malignant tumor of the thyroid. The degree of the malignant condition can apparently be estimated for a given tumor by the extent of its departure from the papillary pattern; the greater the extent of this departure, the more malignant the tumor and the prognosis is thereby equally grave. The study suggests that a favorable outcome can be anticipated only in the papillary form (46 per cent) and the malignant adenomas (24 per cent). The presence of diffuse infiltration by polymorphonuclear leukocytes is of grave prognostic import in any malignant tumor of the thyroid, regardless of its pathologic pattern.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Heart Journal, London

1: 187-268 (July) 1939

Alcoholic Beriberi Heart. A. M. Jones and C. Bramwell.—p. 187.
*Drug Treatment of Hyperpiesia. W. Evans and O. Loughnan.—p. 199.
Electrocardiograph Electrolytes. G. H. Bell, J. A. C. Knox and A. J. Small.—p. 229.
Sir James Mackenzie's Heart. D. Waterston, with clinical history by J. Orr, and notes on pathologic histology by D. F. Cappell.—p. 237.
Cardiac Myxoma: Clinical and Pathologic Study. R. E. M. Fawcett and E. M. Ward.—p. 249.
Standardization of Methods of Measuring Arterial Blood Pressure. Joint Report of the Committees Appointed by the Cardiac Society of Great Britain and Ireland and the American Heart Association.—p. 261.

Drug Treatment of Hyperpiesia.—Evans and Loughnan observed the effect of thirty-three often used preparations on the blood pressure and symptoms of seventy patients with hyperpiesia (essential hypertension). The preparations were various and included nitrites, iodides, sedatives, xanthine and choline derivatives, vegetable extracts and hormones. Each medicament was prescribed in optimal doses for test periods of a fortnight, and at the end of each period the patient was reexamined, when the blood pressure was recorded under the same unvarying and standard conditions and any change in symptoms was noted. Control test periods were instituted for each patient, when an inert placebo mixture was the only treatment given. After allowance had been made for the tendency to obtain high blood pressure readings at the first and possibly at the second examination, and for the natural variation, and when the results from the tested drugs were compared with those from a placebo, the authors found that none of the thirty-three preparations produced hypotensive effects in patients with hyperpiesia. With regard to symptomatic improvement, only six of the drugs (bismuth subnitrate, iodine and iodide, bromide, soluble phenobarbital, potassium thiocyanate and a preparation of theobromine and phenobarbital) on an average relieved symptoms rather more than did the placebo. The sedative drugs seemed to have value in temporarily relieving nervous symptoms when these were prominent. These negative results, the authors state, should not have any bearing on the management of hypertensive heart disease including heart failure, when drug treatment can often be seen at its best. Their negative results with drugs in uncomplicated hyperpiesia do not make it less desirable that the patient should remain under medical supervision. It is obvious that a patient should not regard his symptoms as closely related to the height of his blood pressure. Medical attention must be devoted to the alleviation of symptoms when they arise and to correcting faults in living, and particularly to the adoption of timely active measures when symptoms or signs of heart failure first appear. Time will show whether surgical measures are a practicable means of lowering blood pressure and of lessening symptoms in hyperpiesia. Meantime a clearer insight into the origin of hypertension must precede its successful treatment with drugs.

British Journal of Tuberculosis, London

33: 125-176 (July) 1939

Assessment of Pulmonary Tuberculosis. C. Wall.—p. 133.
Pericardial Effusion in Infancy: Problem in Diagnosis. M. Davidson.—p. 138.
Evidence for Incidence of Tuberculosis in Ancient Egypt. A. J. E. Cave.—p. 142.
Seasonal Variation in Tuberculous Lesions. C. Clayson.—p. 152.
Tuberculosis of Mouth: Review, with Report of Case of Chronic Miliary Tuberculosis Complicated by Condition. C. Cameron.—p. 157.

British Medical Journal, London

2: 51-98 (July 8) 1939

Sleep: Normal and Pathologic. W. R. Brain.—p. 51.
*Treatment of Experimental Tuberculosis with Sulfonamide. K. Birkhaug.—p. 54.
Typhoid Endotoxoid Vaccine: Review of Results of Preventive Inoculation in an Inoculated Population of 400,000. E. Grasset.—p. 58.
Sudden Blindness. J. Minton.—p. 61.
Neuroses Among Combatant Troops in the Great War. F. Dillon.—p. 63.

Treatment of Experimental Tuberculosis with Sulfonamide Derivatives.—Birkhaug states that the parenteral daily injection of a sulfonamide derivative seems to exert a significant inhibitory action on the development of a bovine tubercle bacillus infection of guinea pigs. The inhibitory action appears to be referable to the in vivo bacteriostatic effect of sulfonamide derivatives on the growth of the tubercle bacillus. As sulfonamide derivatives exert only an incomplete bacteriostatic effect on the tubercle bacillus, further investigations should be carried out with new derivatives of sulfonamide. Such investigations are now in progress with sulfapyridine.

2: 99-154 (July 15) 1939

Recent Advances in Vaccine Therapy. A. Fleming.—p. 99.
Dermatitis from Sulfonamide Compounds. D. Erskine.—p. 104.
*Gastroscopic Study of Radiologically Negative Dyspepsia. E. Bulmer.—p. 108.
Problems of Chance in Medicine and Research. L. J. A. Loewenthal and W. A. Wilson.—p. 110.
Management of Frank Breech Presentation. V. Mary Crosse.—p. 113.

Gastroscopic Study of X-Ray Negative Dyspepsia.—Bulmer states that in 1,575 "gastroduodenal" cases, culled from nearly 10,000 new outpatients, an indefinite diagnosis was made in 589 instances (38 per cent). Using the Wolf-Schindler gastroscope, 147 patients with x-ray negative or inconclusive dyspepsia have been studied. In sixty-six cases no abnormality was found, but some abnormality may be present. An increasing experience of gastroscopy has made the author increasingly reluctant to accept a negative observation as significant. The contractions of the pylorus still arouse wonder, but it is tinged with apprehension when the lesser curvature of the antrum refuses to unfold itself: in one of his apparently normal cases an unseen ulcer perforated there. Other blind areas exist, and an ulcer known to be present may not be seen by the gastroscopist. The diagnosis of chronic gastritis was made in sixty cases and the author demands a gross departure from the normal before so diagnosing a case. The gastroscopic observations in the other twenty-one cases of x-ray negative or inconclusive dyspepsia were failure to make an adequate examination in nine, gastric ulcer in eight and one each of simple ulcer later shown to be an ulcer-cancer, curious abnormality later shown to be an ulcer, cancer suspected (not found at operation) and inoperable cancer. Therefore the gastroscope has proved to be of great value in the routine investigation of this type of dyspepsia. Chronic gastritis can be diagnosed with certainty only by gastroscopy, and four case histories are given to emphasize the difficulties of clinical diagnosis.

Journal of Endocrinology, London

1: 1-116 (June) 1939

Seasonal Changes in Ovulation Response of Xenopus Laevis to Methyl Testosterone. H. A. Shapiro.—p. 1.
Effects of Extracts of Pregnant Mare Serum and Human Pregnancy Urine on Reproductive System of Hypophysectomized Male Rats. S. H. Liu and R. L. Noble.—p. 7
Effects of Extracts of Pregnant Mare Serum and Human Pregnancy Urine on Reproductive System of Hypophysectomized Female Rats. S. H. Liu and R. L. Noble.—p. 15.
Comparative Effects of Certain Gonadotrophic Extracts on Ovaries of Normal and Hypophysectomized Rats. R. L. Noble, I. W. Rowlands, M. H. Warwick and P. C. Williams.—p. 22.
Depression of Hypophysial Activity by Implantation of Tablets of Estrone and Estradiol. Ruth Deanesly.—p. 36.
Assay Method for Progesterone Based on Decidual Reaction in Rat. E. B. Astwood.—p. 49.
Observations on Growth (Chondrotrophic) Hormone and Localization of Its Point of Attack. J. Freud, L. H. Levie and D. B. Kroon.—p. 56.
Placental Activity in Mouse in Absence of Pituitary Gland. W. H. Newton and Naomi Beck.—p. 65.
Methods of Extracting Compounds Related to Steroid Hormones from Human Urine. N. H. Callow, R. K. Callow, C. W. Emmens and S. W. Stroud.—p. 76.
Effect of Administration of Testosterone Propionate on Urinary Excretion of Compounds Allied to Steroid Hormones. N. H. Callow, R. K. Callow and C. W. Emmens.—p. 99.
Influence of Subcutaneous Implantation of Tablets of Solid Insulin on Blood Sugar Level of Rabbit. A. S. Parkes and F. G. Young.—p. 108.

Journal of Hygiene, London

39: 345-470 (July) 1939. Partial Index

Notes on Typhus Fevers in Kenya. J. I. Roberts.—p. 345.
Effects of Morphine, Diacetylmorphine and Some Related Alkaloids on Alimentary Tract: Part I. Stomach and Pylorus. G. N. Myers.—p. 375.
Id.: Part II. Small Intestine and Ileocolic Sphincter. G. N. Myers.—p. 391.
Incidence of Quartz and Sericite Particles in Siliceous Residues in Silicotic Lungs. J. Davson.—p. 405.
Influence of Germicides on Dehydrogenases of Bacteria Coli: Part. I. Succinic Acid Dehydrogenase of Bacteria Coli. G. Sykes.—p. 463.

Journal of Laryngology and Otology, London

54: 379-442 (July) 1939

*Double Injury to the Ear. T. De Szentlörinczi-Liebermann and G. Kelemen.—p. 379.
Black Hairy Tongue. G. Swinburne.—p. 386.

Double Injury to the Ear.—De Szentlörinczi-Liebermann and Kelemen report a case in which a woman, owing to a fall on the head from a height and the simultaneous penetration of a hairpin into the ear, sustained a double injury. The fall caused a fracture of the middle and inner ear, whereas the pin penetrating into the ear brought about a luxation of the stapes. Death occurred after three weeks. Dissection, completed by microscopic investigation of the petrous bone, showed that the opening of the oval window, caused by luxation of the stapes, was blocked by granulations. No symptoms of meningitis were observed either clinically or as a result of dissection. Death occurred because of increasing intracranial pressure caused by a hematoma in the scala posterior. This hematoma followed a rupture in the wall of the sinus and constantly increased in volume as irrepressible vomiting pressed fresh quantities of blood through the ruptured sinus. The double nature of the injury was clearly traceable on microscopic examination.

Journal of Pathology and Bacteriology, Edinburgh

49: 1-272 (July) 1939. Partial Index

Argentaffine Cells and Pernicious Anemia. W. Jacobson.—p. 1.
*Incidence and Pathogenesis of Myocardial Lesions in Subacute Bacterial Endocarditis. S. De Navasquez.—p. 33.
Silicosis of Spleen: Study of Silicotic Nodule. T. H. Belt.—p. 39.
Effect of Cholesterol and of Serums Contaminated with Bacteria on Hemolysins Produced by Hemolytic Streptococci. L. F. Hewitt and E. W. Todd.—p. 45.
Transmission of Yellow Fever Virus to Monkeys by Mouth. G. M. Findlay and F. O. MacCallum.—p. 53.
Hemoglobin Metabolism in Chronic Infections. Janet M. Vaughan and M. F. Saifi.—p. 69.
Clinical Severity of Diphtheria in Certain Cities in Great Britain. H. D. Wright.—p. 135.
Production of Toxin by Bacillus Sordellii (Clostridium Sordellii) in Comparison with Other Clostridia. L. E. Walbum and G. C. Reymann.—p. 185.
Significance of Myocardial Scars in Human Heart. T. E. Lowe.—p. 195.
Argentaffine Carcinoma (Carcinoid Tumor) Arising in Ovarian Teratomas: Report of Two Cases. M. J. Stewart, R. A. Willis and G. S. W. de Saram.—p. 207.
Combined (Simultaneous) Immunization Against Tetanus. L. Otten and I. P. Hennemann.—p. 213.
*Pathologic Significance of Megaloblast. M. C. G. Israëls.—p. 231.
Studies on Experimental Herpes Infection in Mice, Using Chorio-Allantoic Technic. F. M. Burnet and Dora Lush.—p. 241.

Myocardial Lesions in Endocarditis.—De Navasquez discusses only cases of subacute bacterial endocarditis due to Streptococcus viridans. In Streptococcus viridans endocarditis, pyemic abscesses in the myocardium or elsewhere are usually absent and embolic lesions, when encountered, do not usually suppurate. The author attempts to determine the characters, frequency and mode of origin of the myocardial lesions in subacute bacterial endocarditis which could be claimed to be in any way specific. The only abnormalities observed were those attributable to subacute bacterial endocarditis. These fall into two groups: (1) vascular, confined to the arteries, arterioles or capillaries and affecting either the lumen or the wall or both and (2) extravascular, consisting mainly of foci of polymorphonuclear leukocytes, with or without necrosis of the parenchyma. Myocardial lesions were encountered in nineteen of twenty cases of subacute bacterial endocarditis. These lesions develop as a result of embolism of the coronary arteries or arterioles by fragments of vegetations which vary in size and bacterial content. They are specific only in that they show evidence of embolism and polymorphonuclear cell reaction. No relation was demonstrated to the degree of cardiac failure, the heart valve affected, the character of the vegetation or the duration of the disease. In view of its ambiguity, it is suggested that the term "Bracht-Wächter body" should no longer be employed.

Pathologic Significance of Megaloblast.—Israëls studied the morphology of the erythroblastic cells obtained by biopsy from human bone marrow in hyperplastic conditions of the erythropoietic tissue and he defines the types of cells appearing. True megaloblasts occur only when the hyperplasia is the result of lack or imperfect working of the anti-pernicious anemia liver principle. In all other conditions, cells of the normoblast series are present. There are also certain primitive cells usually present in all types of hyperplasia, the proerythroblasts and hemocytoblasts. The normal development of the erythrocytes probably proceeds from hemocytoblasts to proerythroblasts and then to normoblasts of varying degree of maturity. The megaloblasts also develop from the proerythroblasts and then follow their own line of development to mature as erythrocytes. The megaloblasts have no place in the development of normal erythrocytes in extra-uterine life; they appear only when the proper activity of the liver principle is in abeyance. So long as the liver principle is normally available, demands for increased erythrocytes, whatever their cause, are met by proliferation of cells of the normoblastic series.

Lancet, London

2: 61-112 (July 8) 1939

Acute Obstruction of Small Intestine. R. L. Holt.—p. 61.
Mechanism of Diabetes Mellitus. H. P. Himsworth.—p. 65.
*Parenteral Therapy with Sulfapyridine Soluble. W. F. Gaisford, G. M. Evans and W. Whitelaw.—p. 69.
Pneumonia Complicating Hematemesis: Treated with Sulfapyridine Soluble. R. Coope and E. Leather.—p. 72.
Pneumococcic Meningitis: Review of Thirty-Nine Fatal Cases and Report of Recovery After Administration of Sulfapyridine Soluble. J. V. Cable.—p. 73.
Lithotomy-Trendelenburg Position for Resection of Rectum and Lower Pelvic Colon. O. V. Lloyd-Davies.—p. 74.
Leuko-Erythroblastic Anemia Resembling Acholuric Jaundice. H. C. Lucey.—p. 76.

Parenteral Therapy with Sulfapyridine Soluble.—Gaisford and his co-workers found that sulfapyridine in a 33⅓ per cent solution of sodium salt is an adequate preparation when it is advisable to use the drug parenterally. They aver that clinically it is no more toxic than sulfapyridine, is not unduly painful after injection, is rapidly absorbed and excreted, and is less likely to cause vomiting than sulfapyridine given orally. In their experience (in various pneumococcic infections) intramuscular injection is preferable to intravenous injection, as it is less liable to cause reaction and vomiting and gives an equally satisfactory concentration in the blood. It is essential that the injection be given intramuscularly and not subcutaneously, or nonabsorption and local necrosis may take place. Although they have treated only thirty-three patients so far, the results, the authors believe, appear to justify its use in selected cases, either when there is a mass infection or when sulfapyridine causes persistent vomiting. It is not intended to replace the oral preparation. A satisfactory scheme is to give from four to six injections of 3 cc. at intervals of four hours. These may be followed by smaller doses of sulfapyridine orally until the temperature falls. Such a system is less likely to cause continued vomiting in susceptible patients than the large initial dosage in general use at present. The drug may be safely given to children and babies in appropriately reduced dosages.

2: 113-170 (July 15) 1939

Surgical Treatment of Arterial Hypertension. P. B. Ascroft.—p. 113.
Mechanism of Diabetes Mellitus: II. Control of Blood Sugar Level. H. P. Himsworth.—p. 118.
*Cyanosis Caused by Sulfonamide Compounds. D. Campbell and T. N. Morgan.—p. 123.
Effect of Sulfanilamide on Blood in Scarlet Fever. Jane O. French.—p. 127.
Fractured Patella Treated by Excision of Fragments. H. Dodd.—p. 130.
*Complete Freedom from Dental Caries: Comparative Study of Twenty-Five Children. H. G. Miller and D. M. R. Crombie—p. 131.

Cyanosis Caused by Sulfonamide Derivatives.—Since cyanosis of varying degree has been a frequent symptom following treatment with the sulfonamide group of drugs, Campbell and Morgan attempted to assess the therapeutic value of methylene blue, favorably reported on by others, in the treatment of methemoglobinemia and sulfhemoglobinemia. Four cases illustrating the value of methylene blue in pneumonia methemoglobinemia following treatment with sulfapyridine are cited. The authors state that it can hardly be argued that the results obtained in these cases were due to a natural and spontaneous remission in the severity of the cardinal symptom, because they had previously found that, when methemoglobinemia developed during treatment with sulfapyridine, the pigment could be detected in the blood four or five days after all trace of the drug had disappeared from the blood stream. It is justifiable, therefore, to conclude that methylene blue actively converts methemoglobin into hemoglobin. Methylene blue has a similar action on the methemoglobinemia produced

by the administration nitrites. The dye is active when given by mouth. It is also slowly excreted. A prolonged effect can therefore be obtained by giving it by mouth in divided doses several times a day. In view of its action in preventing methemoglobinemia and its attending cyanosis the authors suggest that it might be worth while considering the advisability of giving it as a routine along with sulfapyridine in conditions in which prolonged treatment is necessary. The efficacy of methylene blue was also tried in two cases of sulfhemoglobinemia which developed after the administration of sulfanilamide. The dye was given intravenously and orally but was without effect. It did not prevent the development of sulfhemoglobinemia when it was administered along with sulfanilamide.

Complete Freedom from Dental Caries.—In an endeavor to trace some of the grosser causal factors of dental caries, Miller and Crombie examined twenty-five children from 10 to 14 years of age with caries-free mouths and no history of caries in the permanent dentition and compared them with an equal number of children showing gross caries but similar in other respects. They found that certain factors which were apparently associated with freedom from dental caries were the following: (1) good family dental history (not apparently of such significance as good general hygiene and diet), (2) careful infant feeding, especially breast feeding, and, (3) probably above all, absence of severe illness and an early incidence of infectious fever. No difference of present economic status was demonstrable between the two groups, but a point of importance appeared to be that children with bad teeth were often the younger members of a family, whereas those with good teeth were frequently first children. In this series of cases irregular dentition and inadequate oral hygiene did not appear to exercise any unfavorable effect on the degree of freedom from caries.

Medical Journal of Australia, Sydney

2: 51-86 (July 8) 1939

Search for Immunologic Relationship Between Q Fever and Other Rickettsioses. F. M. Burnet, Mavis Freeman, E. H. Derrick and D. J. W. Smith.—p. 51.
Preeclamptic Toxemia. I. Buzzard.—p. 55.
Summary of Modern Views on Female Sex Hormones and Their Scope in Therapy. A. J. Cunningham.—p. 58.
Difficulties in Third Stage of Labor, with Special Reference to Retained Placenta and Mojon-Gabaston Technic. W. K. McIntyre.—p. 62.
Intracutaneous Injection of Small Measured Volumes of Liquid. D. Anderson.—p. 68.

2: 87-122 (July 15) 1939

Making Medical Men. A. Newton.—p. 87.
Juvenile Delinquency. J. McGeorge.—p. 94.
The Difficult Child. D. W. H. Arnott.—p. 105.

Proceedings of Royal Society of Medicine, London

32: 1023-1190 (July) 1939

Histology and Histopathology of Dental Innervation. R. Bradlaw.—p. 1040.
Comparative Study of Innervation of the Gum. D. Stewart and W. Lewinsky.—p. 1054.
Results of Treatment of 400 Cases of Lobar Pneumonia with Sulfapyridine. W. F. Gaisford.—p. 1070.
Treatment of Malaria in Military Population with Synthetic Preparations. S. Smith.—p. 1077.
Experience with Synthetic Drugs in Treatment of Malaria. F. M. Lipscomb.—p. 1082.
Tumors of Lateral and of Third Ventricles. G. Jefferson and H. Jackson.—p. 1105.
*Radiotherapy of Intracranial Tumors, with Special Reference to Treatment of Pituitary Tumors. O. Orley.—p. 1137.
Familial Hepatitis and Chronic Jaundice. R. Debré.—p. 1173.
History of Clinical Medicine (Principally of Clinical Teaching) in the British Isles. H. Rolleston.—p. 1185.

Roentgen Therapy of Intracranial Tumors.—Orley reviews the results obtained in the roentgen treatment of intracranial tumors. He states that most of the gliomas are sensitive to x-rays, but the degree of sensitivity varies with the histologic type in the descending order: medulloblastoma, ependymoma, astrocytoma and glioblastoma multiforme. The oligodendroglioma is resistant to the x-rays. Of the vascular tumors the hemangioblastomas should be treated by operation and postoperative irradiation, while the malformations should receive irradiation alone. The meningiomas are resistant tumors. The evolution of pituitary adenomas can be divided into three stages: endocrine, visual and tumoral. The endocrine phase should be treated with radiation, the tumoral phase with surgery and the treatment of the visual phase should be determined by the circumstances. Patients undergoing roentgen therapy should be watched closely and surgical intervention undertaken when required. The best results follow combined treatment.

Quarterly Journal of Medicine, Oxford

8: 185-276 (July) 1939

Cerebral Blood Flow in Arterial Hypertension, Arteriosclerosis and High Intracranial Pressure. D. Williams and W. G. Lennox.—p. 185.
*Effect of Pituitary Thyrotropic Extract in Subjects with Low Basal Metabolic Rates. E. P. Sharpey-Schafer and I. Schrire.—p. 195.
*Treatment of Chronic Hypoparathyroidism. I. A. Anderson and A. Lyall.—p. 209.
Differential Diagnosis of Forms of Basophilism (Cushing's Syndrome), Particularly by Estimation of Urinary Androgens. A. C. Crooke and R. K. Callow.—p. 233.
*Causation of Low Blood Sugar Curve in Celiac Disease. T. Crawford.—p. 251.
Rheumatic Heart Disease as Met With in Hospital Practice in Ceylon. P. B. Fernando.—p. 261.

Effect of Pituitary Extract on Metabolism.—Sharpey-Schafer and Schrire studied the effect of intramuscular injection of pituitary thyrotropic extract on twenty-two normal subjects without disease of the endocrine glands, three with myxedema, one cretin and nine with low basal metabolic rates but lacking the typical signs of myxedema. The twenty-two subjects (nearly every one was suffering from peptic ulcer, sciatic pain or some surgical condition) without exception showed a normal response to the injection of thyrotropic extract. Every subject, except two, complained of malaise. Headache was usual, and some tenderness was felt in the region of the neck. Every subject showed enlargement of the thyroid. The onset of symptoms was usually on the third or fourth day of injection and on ceasing injection the symptoms subsided rapidly, so that in forty-eight hours the thyroid had returned to nearly its normal size, though the pulse rate often remained rapid for several days longer. Creatine was excreted in abnormal amounts in the urine. The basal metabolic rate became elevated. Five subjects with various disorders of the endocrine system, but without evidence of thyroid disease, gave the same response as the twenty-two normal subjects when injected with thyrotropic extract. In each case the basal metabolic rate, the electrocardiogram, the blood cholesterol and the circulation time were within normal limits. The three subjects with myxedema and the one cretin showed no response to the injection of thyrotropic extract. No alteration was observed in the clinical state, the creatine excretion or the basal metabolic rate. Five subjects with a low basal metabolism responded normally to the injection of thyrotropic extract and in four (one of acromegaly) there was no response, although there is considerable evidence that they have functioning thyroids. These results the authors believe show that a reliable preparation of thyrotropic extract may be used to investigate the function of the thyroid in man. Its further use may help to clarify that indefinite group of cases which have low basal metabolic rates but lack other signs of thyroid deficiency.

Treatment of Chronic Hypoparathyroidism.—Anderson and Lyall determined the calcium and phosphorus metabolism in three cases of postoperative parathyroid deficiency, first on a high calcium diet with a relatively high phosphorus intake and then on a low phosphorus diet in which the calcium intake was maintained at the previous high level by appropriate supplements of calcium lactate. Three subjects, serving as controls, with normal parathyroid function and calcium metabolism were studied in the same way. In the three cases of parathyroid deficiency the serum calcium could be raised to and maintained at a normal level by the administration of the diet low in phosphorus together with large doses of calcium lactate. The primary importance of this reduction in phosphorus intake was illustrated in two cases in which the same or even a greater calcium intake had no effect on the depressed serum-calcium level as long as the phosphorus intake remained high. The suggested optimal level of phosphorus intake is from 0.5 to 0.65 Gm. daily, depending on the body weight of the individual. The results of the balance experiments in these cases indicate that the improvement in the blood chemistry produced by a reduction of the phosphorus intake cannot be explained by an increased retention of calcium in the body or

a loss of phosphorus from the body. The rise in serum calcium seems rather to be secondary to the fall in serum phosphorus, which in its turn appears to be the result of a diversion of phosphorus from the body fluids to some other site in the body rather than of any loss of phosphorus from the body. The amount of phosphorus excreted by the kidneys in the three cases of parathyroid deficiency on a high phosphorus intake was as great as in the three normal subjects on a similar phosphorus intake. Normal subjects have a negative phosphorus balance during the first twelve days after the phosphorus intake is reduced from 2 to 0.5 Gm. daily, the calcium intake being 2 Gm. daily throughout. Under similar conditions patients with parathyroid deficiency, unless there is complicating renal disease, remain in positive phosphorus balance, the excretion of phosphorus by the kidneys being less than that of normal subjects on the reduced phosphorus intake. Tenth normal hydrochloric acid therapy does not adversely affect the calcium balance of patients with parathyroid deficiency, provided the calcium intake is adequate and sufficient phosphorus is being given to maintain phosphorus equilibrium. The minimal dose of vitamin D necessary to raise the serum calcium to a normal level in parathyroid deficiency appears to lie between 30,000 and 45,000 international units daily. The higher dose is effective even when the phosphorus intake is not reduced. There is thus evidence of a decreased excretion of phosphorus by the kidneys in parathyroid deficiency only when the phosphorus intake is low.

Cause of Low Blood Sugar Curve in Celiac Disease.—Crawford performed the intravenous dextrose tolerance test in twelve established cases of celiac disease, eleven of which showed a typical low oral blood sugar curve. No significant difference was found between the curves in the celiac cases and curves from normal subjects; and in five cases no difference was observed between curves obtained during active and latent phases of the disease. Insulin sensitivity tests in six of the cases gave results closely similar to those obtained from six normal subjects. From these results the author concludes that there is no abnormality of intermediate carbohydrate metabolism in cases of celiac disease; and, by exclusion, it seems certain that the low blood sugar curve of celiac disease must be due to delayed or defective absorption of carbohydrate from the intestine. This conclusion is presumably applicable to other forms of idiopathic steatorrhea as well as to celiac disease.

Chinese Medical Journal, Peiping

55: 505-594 (June) 1939

Carcinoma in Osteomyelitis. C. M. Meng.—p. 505.
Intussusception in Adults: Report of Eight Cases. C. S. Huang.—p. 514.
Pellagra and Its Treatment with Nicotinic Acid. H. C. Hou.—p. 528.
Trichinella Infection in Rats in Fukien. C. C. Tang.—p. 537.
Studies on Certain Problems of Clonorchis Sinensis: VII. Further Advance in Study of Life Cycle of Clonorchis Sinensis. H. F. Hsü.—p. 542.
Development of Health Centers. T. F. Huang.—p. 546.
*Taenia Infection: Report Based on Stool Examinations of 56,286 Patients in Peiping Union Medical College. L. S. Wu.—p. 561.
Note on Coincidence of Human Kala-Azar and Canine Leishmaniasis with Cutaneous Lesions in a Household. E. A. Ho.—p. 566.

Taenia Infection.—Wu points out that the stool examinations of 56,286 patients, done at the Parasitological Laboratory of the Peiping Union Medical College, revealed 337 cases positive for Taenia infection, giving a percentage of 0.6. The Taenia species was not determined in 153 cases, in 156 cases Taenia saginata was found and in the remaining twenty-eight cases Taenia solium. The relative frequency of Taenia solium to Taenia saginata was 1:5.6. Among the twenty-eight cases of intestinal infection of Taenia solium, seven cases were reported as presenting also a somatic infection with Cysticercus cellulosae, and two of these showed cerebral cysticercosis. The Taenia infection rate was higher in males (224) than in females (113). The youngest patient with Taenia infection was a child of 1 and the oldest was 76 years of age. The infection was highest among the students and lowest in farmers and children. The infection rate of foreigners in China was, so far as could be judged, only slightly lower than that of the Chinese. The majority of the patients came from the vicinity of Peiping. However, it seems that Taenia infection occurs in all parts of China.

Archives des Maladies du Cœur, Paris

32: 657-768 (July) 1939

*B_1 Hypovitaminosis and Cardiopathies: Role of Deficiency in Vitamin B_1 in Pathogenesis of Cardiovascular Disturbances in Chronic Alcoholic Addicts. G. Bickel.—p. 657.
Phonarteriography. G. Giraud, H. Barati and R. Loubatières.—p. 669.
Cardiometric Study of Tonicardiac Properties of Some Sympathicomimetic Amines. R. Charlier.—p. 690.
Electrocardiogram in Precordial Derivations Registered Roentgenologically: Analytic Study of Ventricular Complex. A. Pruche.—p. 711.
Electrocardiogram of Patients with Hypertension. R. Lévy.—p. 730.

B_1 Hypovitaminosis and Cardiopathies in Chronic Alcoholic Addicts.—Bickel demonstrates that in a large number of patients with chronic alcoholism there exist circulatory disorders independent of all valvular, vascular or renal disorders. These disturbances consist chiefly of tachycardia, cardiac irritability, dyspnea of effort, dilatation of the heart, arterial hypotension and occasionally acute asystole. They are accompanied by only slight anatomic lesions and can be considered, at least in their first phases, as purely functional disturbances. The author presents a series of arguments which indicate that the cardiovascular disturbances of patients with chronic alcoholism may be caused by a deficiency of vitamin B_1. This deficiency of vitamin B_1 is due partly to the diminution in the total food intake of alcoholic addicts and to the impairment of their digestive tract, which hinders the normal absorption of certain alimentary substances. It is due even more to the considerable augmentation of the requirements of vitamin B_1 on the part of the organism of alcoholic addicts in comparison with the healthy organism. Vitamin therapy is likely to produce favorable effects on the cardiac disturbances of alcoholic addicts. These results are entirely comparable to those obtained in alcoholic polyneuritis. However, whereas the effects of the vitamin therapy are rapid and complete when the cardiovascular disturbances are recent, they are no longer obtainable in the old cases in which definite organic changes have replaced the functional and reversible changes of the early stages.

Journal de Chirurgie, Paris

54: 145-288 (Aug.) 1939

Microsporadic Hyperthyroidism. A. Jentzer.—p. 145.
*Attenuated Pancreatitis. J. Meyer-May.—p. 174.
Ligation of Carotids in Dissection of the Neck for Cancer. M. Bérard and M. Dargent.—p. 197.
Amputation of a Stenosing Tumor of the Rectum. Guillermo.—p. 211.

Attenuated Pancreatitis.—According to Meyer-May, there were admitted to the Surgical Clinic of the Medical School at Hanoï (French Indo-China) in the period of 1936 to 1938 inclusive twenty-seven cases of acute nonhemorrhagic pancreatitis. This type of pancreatitis, termed by Delbet "attenuated pancreatitis," differs from the acute hemorrhagic type in a tendency to recurrent attacks and to chronicity. Diagnosis in nine of his cases was verified by gross inspection at operation and by biopsy of the pancreas. The study also includes a group of six cases of gastroduodenal ulcer exhibiting clinical and secretory signs of pancreatitis, the existence of which was revealed at operation. A contrast study was made of the pancreatic ferments from the duodenal juice of twenty-nine healthy persons. Biliary tract involvement was present in only one case. Pancreatitis existed as a complication in one out of every five cases of gastroduodenal ulceration. Intestinal parasitism was present in every case, the common finding being that of Ascaris or Tricocephalus. The author believes that the secretion of the parasites may act as an etiologic factor in the causation of this form of pancreatitis. The microscopic studies revealed two types of a pancreatic lesion: the classic edematous pancreatitis and the sclerotic chronic sclerolipomatosis. The author has never encountered a case of hemorrhagic pancreatitis. He does not regard the edematous form as a precursor of hemorrhagic pancreatitis. The author stresses particularly the finding of hyperglycemia in every case. Injection of insulin in these cases was always followed by lowering of hyperglycemia, alleviation of pain and improvement in the general state. Another important laboratory finding was the constant lowering of the pancreatic ferments in the duodenal juice, particularly that of lipase. The author feels on the basis of his experience that insulin treatment will obviate the necessity of performing a cholecystotomy in most of these cases. The insulin is administered in doses of from 15 to 45 units daily until the blood sugar level returns to

normal. He does not consider the objection that these cases may be confused with acute perforating ulcer demanding an immediate operation as valid because the two syndromes present different pictures. The pancreatic crisis described is characterized by agonizing epigastric pain but, unlike a perforating ulcer, it presents only a moderate rigidity of the abdominal wall and a characteristic, almost pathonomonic, sign of distention of the transverse colon. There is a characteristic hyperglycemia and a diminution of the pancreatic ferments in duodenal juice. There is a similarity, according to the author, between the crises caused by pancreatic insufficiency described and the clinical picture of crises due to adrenal insufficiency.

Journal d'Urologie Médicale et Chirurgicale, Paris

48: 97-192 (Aug.) 1939

*Urethrovesiculodeferential Reflux. J. Perves and H. Duvergey.—p. 97.
Perineal Ectopic Testis. A. Puigvert Gorro.—p. 114.
Culture of Urines Collected After Massage of Prostate and of Seminal Vesicles in the Detection of Chronic Gonorrhea and as Test of Cure. S. Goligorsky.—p. 118.

Urethrovesiculodeferential Reflux.—Perves and Duvergey designate as urethrovesiculodeferential reflux the passage of a liquid, of urine, sperm or injected substance, from the posterior urethra into the genital system. Normally the orifices of the ejaculatory ducts are physiologically closed and impermeable for injections made into the canal. Serial urethrographies on normal urethras never show the passage of opaque liquid into the genital apparatus of man. Repeated attempts on cadavers either with iodized oil or with colored liquid have been negative; injecting these liquids into the urethra under great pressure never produces reflux into the vesiculodeferential system but rather a rupture of the mucosa with passage into the corpus spongiosum and the venous system of the urethra. As far as the authors know, Brach is the only one who produced injection of the seminal vesicles by way of the urethra in two cadavers. But although it is a demonstrated fact that healthy ejaculatory ducts are impermeable and that urethrovesiculodeferential reflux is never produced in normal urethras, it appears that certain acute or chronic infections of the posterior urethra which are accompanied by a wide opening of the orifices of the ejaculatory ducts can explain this injection of the seminal passages by reflux. After discussing similarities between urethrovesiculodeferential reflux and vesicorenal reflux, the authors present a table in which they list all cases of urethrovesiculodeferential reflux that they collected from the literature. The table lists the name of the author, the injected organ and the cause of the reflux. The table indicates that in five of the twenty cases urethritis and prostatitis was the cause, in nine cases genital bacillosis and in six cases prostatectomy. Further they give detailed descriptions of the four cases which they observed. The first two are related to epididymitis, the bacillary character of which was probable in one and certain in the other. In these two cases the vesicles showed injection. In the other two cases the reflux appeared after prostatectomy; in the first one of these the reflux was active, appearing only in the course of mictional urethrography, otherwise the patient complained of testicular pains on urinating; in the last case the reflux was passive. The passive and active types of reflux correspond to two different pathogenic explanations. In the great majority of cases the reflux is passive; that is, it is a purely mechanical factor due to abnormal permeability of the ejaculatory orifices and it develops in the course of retrograde urethrography under the influence of the pressure of injection. In certain conditions, however, an active reflux exists which necessitates for its production contractions of the bladder.

Presse Médicale, Paris

47: 1117-1124 (July 15) 1939

Vaccinations and the Public. A. Touraine.—p. 1117.
*Importance of Spinal Anesthesia in Pathogenic Diagnosis of Megacolon: Its Eventual Therapeutic Utilization. V. Climesco, P. Sarbu and S. Roman.—p. 1118.

Spinal Anesthesia in Megacolon.—Climesco and his associates report the successful employment of spinal anesthesia in the treatment of megacolon. The patient, a girl aged 12 years, was admitted for fistulous coxalgia but a few days after admission developed digestive disorders evidenced by vomiting, tympanism and prolonged constipation. Clinical examinations coupled with anamnesis of the patient indicated the manifest presence of megacolon of the Hirschsprung type. Spinal anesthesia induced with procaine hydrochloride (0.1 Gm. in an 8 per cent solution) and primarily used to aid plastic intervention by the Hibbs method yielded an unexpected secondary result by normalizing the patient's evacuations for a period of sixteen days. The second administration of the same drug regularized her stools for nearly four months. According to the authors, the value of spinal therapy consists in giving free play to the parasympathetic nerves by paralyzing the sympathetic and thus activating peristalsis of the colon. It has the advantage of simplicity, requires no great surgical skill, forestalls more serious surgery and produces no immediate or delayed sequels.

47: 1141-1156 (July 22) 1939

Importance of Sign of Supraminimal Silent Zone in Diagnosis of Pure Stricture of Aorta or Associated with Aortic Insufficiency. C. Lian and P. Geismar.—p. 1141.
*Acaprin in Treatment of Chronic Malarial Splenomegalies. I. Radvan.—p. 1143.

Acaprin in Malarial Splenomegalies.—Radvan maintains that fever and hypertrophy of the spleen, the most important symptoms of malaria, are not influenced in the same manner by the specific therapy, for, if the fever is rapidly suppressed, the hypertrophy of the spleen frequently persists. In order to counteract the splenic hypertrophy that fails to yield to the specific treatment, the author employed as an adjuvant acaprin, a quinoline preparation. The satisfactory results he obtained with this method induced him to report his experiences with this treatment. The doses employed by him were usually slightly below 1 mg. per kilogram of body weight, 1 mg. per kilogram being the maximal dose. The substance is administered in the form of an aqueous solution by subcutaneous or intramuscular injection. The rhythm and number of injections are fixed in accordance with the reaction of the patient to the medicament. Generally, from two to five injections are given at intervals of from two to three days. As long as fever exists, it is advisable to give first quinine or other antimalarial medicaments. After apyrexia has been established and the parasitic elements have disappeared from the peripheral blood, the author begins treatment with acaprin, which is without danger if the aforementioned doses are not exceeded. It rapidly reduces the size of the splenic tumor and counteracts the splenic pains. Moreover, there follows improvement in the general condition and in the anemia and an increase in the weight of the patient.

Revue de la Tuberculose, Paris

5: 753-880 (July) 1939. Partial Index

Experimental and Therapeutic Study on Action of Genital Hormones on Menstrual Disturbances of Patients with Tuberculosis. Pierre-Bourgeois and Mmes. M. Boquet-Jesensky and Denise Pierre-Bourgeois.—p. 754.
*Procedure of "Reactivation" in Serodiagnosis of Tuberculosis. K. Meyer and Mme. Froyez-Rœderer.—p. 775.
Study of Pleural Endothelioma. E. Sergent and R. Kourilsky.—p. 788.
Roentgenphotography: First Attempts of Application to Detection of Pulmonary Tuberculosis in Army. Fournié and Frezouls.—p. 795.
Roentgenography of Thorax. G. Maingot.—p. 802.
Negative Tuberculin Reactions in Subjects Infected with Tubercle Bacilli. E. Coulaud and Lemanissier.—p. 806.
Vaccination with BCG by Method of Multiple Superficial Punctures. S. R. Rosenthal.—p. 815.
Vaccination with BCG by Cutaneous Scarification. B. Weill-Hallé.—p. 827.
Intravenous Injections of Sodium Benzoate in Treatment of Pulmonary Tuberculosis in Children. P. Lowys, P. Couve and H. Delhumeau.—p. 836.

"Reactivation" in Serodiagnosis of Tuberculosis.—According to Meyer and Froyez-Rœderer, it is well known that the seroreactions for tuberculosis may give negative results in a certain number of cases of established tuberculosis. Most of the patients were persons examined at the beginning of the infection or cachectic persons in a state of anergy, a state in the course of which the cutaneous reaction is likewise negative. But aside from these cases there are others in which, in spite of a favorable general condition, a manifest and progressive tuberculosis is accompanied by a negative seroreaction. The latter nevertheless can become strongly positive when the patients are treated with tuberculin. It is known, for instance, that a small dose of tuberculin which is without effect on

normal guinea pigs or rabbits may give rise to an abundant production of antibodies in tuberculous animals. If in human subjects the conditions are the same, there is a possibility of augmenting the proportion of positive reactions in cases of tuberculosis. This "reactivation" of the seroreaction is effected by the authors by means of the intracutaneous injection of small doses of tuberculin. They employed this method in 100 cases in which the seroreaction was negative, freedom from tuberculosis existing in fifty and osteo-articular or glandular processes of a tuberculous nature being present in fifty. They found that by the injection of small doses of tuberculin it is possible to increase in tuberculous subjects the occurrence of positive seroreactions, the increase being from 87 to 95 per cent in adults and from 70 to 85 per cent in children. In nontuberculous subjects the same procedure is without effect on the subjects with a negative cutaneous reaction, but it provokes a positive seroreaction in more than a third of the persons who have a positive cutaneous reaction. A seroreaction which becomes positive under the influence of tuberculin, although not presenting an absolute indication, can raise suspicion of an active tuberculosis; a reaction that remains negative suggests with considerable probability, particularly in adults, the absence of an active tuberculous process.

Sang, Paris

13: 705-816 (No. 7) 1939

*Glutathione Content of Blood in Polyglobulism, Leukemia and Chronic Erythroblastosis. P. Émile-Weil, A. Aschkenasy and L. Capron.—p. 705.
Summary of Comparative Examinations Concerning Action of Benzene on Leukocytic Reactions. G. Wallbach.—p. 719.
Anemia of Aged Women. M. Faure-Beaulieu, R. Cahen and M. Feld.—p. 739.
Anemia with Bartonella Muris: Aspects and Development, Action of Antianemic Hepatic Factors. M. Lourau, G.-S. de Sacy and A. Arthus.—p. 749.

Glutathione Content of Blood Hemopathies.—Émile-Weil and his associates point out that it has been demonstrated in numerous investigations that glutathione plays an important part in the process of oxidoreduction of the organism. They cite methods by which it is determined in the blood. They made their own investigations with the method of Binet and Weller, which seemed to them the most specific. They studied the glutathione (total, reduced and oxidized) content of the blood of fourteen patients with leukemia and cryptoleukemia, of four with polycythemia, of three with erythroblastosis and one with myeloma. The hemograms of the patients were examined simultaneously and in the majority of them the basal metabolism was likewise determined. They found that in polyglobulism the total glutathione was constantly elevated and seemed to increase with the number of erythrocytes. The amount of oxidized glutathione as well as the glutathionemic quotient, however, varied greatly. The leukemias were likewise characterized by a certain augmentation of the total glutathione, but the augmentation was less pronounced and had no relation to the leukocytosis. The latter, on the other hand, seemed to influence the amount of oxidized glutathione. There was a tendency toward elevation in the myelogenic leukemias, but almost complete disappearance in the lymphatic forms. It was likewise absent in a case of glandular lymphomatosis, whereas, contrary to the true lymphatic leukemias, it was normal or elevated in two cases of splenic lymphomatosis. The erythroblastoses were characterized by the complete absence of the oxidized form. Finally, no relationship could be observed between the glutathione and the basal metabolism on the one hand and the cholesterol content on the other hand.

Schweizerische medizinische Wochenschrift, Basel

69: 697-716 (Aug. 5) 1939. Partial Index

Significance of Pleural Depression. P. Vuilleumier.—p. 697.
Treatment of Articular Distortions. F. Jakob.—p. 700.
*Dihydrotachysterol and Thallium. A. Buschke and W. Konheim.—p. 702.
Positive Indications in Serologic Paternity Tests. F. Ottensooser.—p. 703.

Dihydrotachysterol and Thallium.—After pointing out that the antitetanic preparation dihydrotachysterol influences the calcium metabolism, Buschke and Konheim review its favorable effect on the cataract of tetany. They further state that cataract as well as rachitic changes of the bones has been known to develop in animals which have been treated for long periods with thallium, and they decided to investigate whether the inhibiting effects exerted by thallium on the growth process could be counteracted by medication with dihydrotachysterol. One group of young rats, weighing between 55 and 65 Gm., was given dihydrotachysterol as well as thallium, whereas a control group was given only thallium. It was found that the controls remained much smaller than the animals which in addition had been given dihydrotachysterol. At the end of several months the control animals weighed only 85 Gm., whereas the animals which had received the dihydrotachysterol weighed 250 Gm. Later the authors made the same experiments on two other series of rats and obtained the same results. The experiments prove that dihydrotachysterol is capable of inhibiting the impairment of growth produced by thallium. However, a modification of the hair growth could not be observed. The authors consider it probable that thallium exerts an unfavorable influence also on the parathyroids, which are an important factor in the growth of bones, and that the dihydrotachysterol again promotes the function of the parathyroids as in tetany and tetany cataract. To be sure, it is known that osseous growth is influenced also by the hypophysis, thyroid, thymus and sex organs and it has been determined that the function of these organs is impaired by thallium. Additional metabolic and microscopic studies will be necessary to obtain more information about the relations between thallium and dihydrotachysterol.

Rivista di Patologia e Clin. d. Tubercolosi, Bologna

13: 487-564 (July 31) 1939. Partial Index

*Tuberculous Allergy: Determinations by Intradermal and Skin Reactions with Petragnani Anatuberculin. M. Pellegrini and N. Carinci.—p. 487.
Value of Behavior of Reticulocytes in Pulmonary Tuberculosis in Children. G. Murano and G. Fiordelisi.—p. 498.
Early Tuberculous Infiltration in Children and Adolescents: Importance of Pathogenesis of Phthisis. E. Filla.—p. 517.

Tuberculous Allergy.—Pellegrini and Carinci followed the behavior of tuberculous allergy in a group of 138 adult patients who were suffering from either pleuropulmonary tuberculosis or nontuberculous diseases. Allergy was determined by means of the intradermal and cutaneous reactions to anatuberculin (a tuberculin preparation), which were carried on simultaneously. The intradermal reaction gave positive results in eighty-one cases, in fifty-two of which the skin reaction also gave positive results. Both tests gave negative results (anergy) in fifty-seven cases in the group, including several in which mild forms of chronic pleuropulmonary tuberculosis were present. The author found that a positive cutaneous reaction appears within the first twelve hours in the course of the test, whereas a positive intradermal reaction appears late (regularly it appears after the first twelve hours and in some cases as late as about forty-eight hours in the course of the test). The tests can be simultaneously made without any inconvenience to the patients or any interference with the results. The cutaneous reaction gives positive results only in cases in which the intradermal reaction is going to be strongly positive. It shows florid forms of pleuropulmonary tuberculosis. The test is of value in association with the intradermal reaction as a criterion for evaluation of the evolution of the disease. The more or less intense positivity of the cutaneous reaction shows the more or less acute evolution of the disease. There are various unknown organic factors which may induce diminution of tuberculous allergy (and even cause anergy) in adults with mild chronic pleuropulmonary tuberculosis. There are also various diseases, especially influenza, malaria, cancer and typhoid, which cause anergy. Rheumatic fever stimulates tuberculous allergy. The latter is of the same degree of intensity in rheumatic fever as it is in pleuropulmonary tuberculosis.

Brasil-Medico, Rio de Janeiro

53: 763-782 (July 29) 1939. Partial Index

Vasodilatation of Capillaries Following Compression of Limbs by Rubber Armbands. R. Ferreira.—p. 763.
*Clinical Problem of Migraine in Children. A. Oliveira Lima.—p. 765.

Migraine in Children.—According to Oliveira Lima, allergy is the main etiologic factor of migraine in children. Heredity and constitutional physical factors, or else pathologic factors, are secondary. The condition is more frequent in girls than in boys and again more frequent in girls of a nervous type than in normal girls. The clinical symptoms are those of the prodromal, aural, attack and after-attack periods. The topography, acuteness and evolution of the disease are varied in the

different cases. The main symptom of the attack is the one-sided headache, which appears at regular or irregular intervals with pain of the oppressive, irradiating or neuralgic types and is accompanied by nausea, vomiting and various sensory disturbances. Intolerance to light is more or less acute in all cases. The after-attack stage gradually establishes itself, after an aggravation of the acute symptoms of the attack. It becomes evident by appearance of physical depression, sleep, disturbances of the secretion and elimination of urine, rhinorrhea and general dull pain. In some cases the development of an abortive or equivalent attack prevents development of typical attacks. Chronic headache may be a late sequel of the disease. The treatments consist of any of the three types (1) preventive, (2) symptomatic and (3) after-attack. There are two forms of preventive treatment: that by which patients are advised not to marry persons who are sensitive to the same allergens, and the actual preventive treatment of the patient, which includes proper diet and avoidance of food and ambient allergens to which the patient is sensitive. Symptomatic treatment varies with the type of headache. The following general measures are indicated: To confine the patient to a dark quiet room and to administer drugs of a vasodilating action during the prodromal and aural stages and, during the attack, administration according to proper indications of drugs of vasoconstrictive action, or else analgesics, sedative drugs and especially ergotamine. Caffeine, calcium and some other drugs can be resorted to, following proper indications. The after-attack treatment is a continuation of the administration of the symptomatic treatment with certain modifications. It consists of the proper diet, rest of the patient and administration of either sedatives or else stimulants according to indications.

Revista de la Sanidad Militar, Havana

3: 229-307 (July-Aug.-Sept.) 1939. Partial Index

Intrapleural Chrysotherapy in Insufficient Pneumothorax. B. Cardelle and J. Arias Avellán.—p. 266.
*Endocrine Treatment in Hypertrophy of Prostate. A. Muxó González.—p. 284.

Endocrine Treatment in Prostatic Hypertrophy.—Muxó González administered testosterone propionate to a group of twenty-five patients who had hypertrophy of the prostate of either the first, second or third degree. The group included (1) patients with moderate or no retention of urine and a normal amount of urea in the blood, (2) patients with acute retention and a high amount of urea in the blood and (3) patients with grave retention and general intoxication. The substance was administered by injections, every other day, in doses of 0.025 Gm. for each injection over a period of three or four weeks. The treatment was repeated after an interval of two months in grave cases at the rate of two injections of the mentioned dose for one week (and in rare grave cases for a month). The author concludes that the testosterone propionate treatment diminishes (or else controls) painful difficult urination and frequent urination. Voluntary micturation becomes free, forceful and abundant. Residual urine, azotemia and hypertrophy diminish (and in some cases disappear). The sexual functions and the general condition of the patient improve. The best results are obtained when the treatment is administered early in the development of hypertrophy. The treatment is also of value for the preparation of patients for a partial endoscopic prostatectomy and as a complementary treatment after prostatectomy. The treatment has its proper indications and it is not a substitute for prostatectomy when the latter is indicated. The author points out the advisability of considering the dose of 0.025 Gm. of the substance as the largest to be administered every other day. The administration of a larger dose or of daily doses in the same amount may cause painful erections.

Semana Médica, Buenos Aires

46: 509-564 (March 9) 1939. Partial Index

*Intestinal Intussusception in Infants. A. Lagos Garcia.—p. 521.
Chrysotherapy in Rheumatoid Arthritis. V. H. Richeri and J. Davidovsky.—p. 526.
Myxedema of the Heart. C. Lian Facquet.—p. 559.

Intestinal Intussusception in Infants.—Lagos Garcia resorted to surgical treatment in twenty-nine cases of intestinal intussusception in infants, the majority of whom (eighteen) were breast fed. In all cases there was intermittent colic pain and vomiting. In twenty-seven cases rectal elimination of blood had already occurred when the patients were seen. The tumor could be felt by palpation in twenty cases. The operation was performed as the primary treatment in twenty-seven cases and after failure of the enema of opaque substance with pressure in two cases. The invagination was of the ileocecal type in twenty-one cases and of the ileocolic type in six cases. The twenty-four patients who had the operation before forty-five hours from the beginning of the disease recovered. The five patients who died either had the operation very late or else were extremely young and had acute forms of the disease. In grave cases a given dose of a 10 per cent hypertonic solution of sodium chloride was administered to the patients, intravenously, after the operation. Eventration in one case was the only complication observed in the group. It was successfully treated by a further operation. The author gives the following advice: (1) Resort to the operation early and prevent evisceration, (2) make disinvagination within the abdomen, bringing out of the abdomen only the last portion of the tumor, (3) apply compresses of warm physiologic solution of sodium chloride on the tumor (with the aim of diminishing tension) and (4) perform the operation carefully, rapidly (from fifteen to twenty minutes) and without traction. He concludes that the surgical treatment gives satisfactory results in intestinal intussusception in infants. The danger of the treatment has been exaggerated. The treatment is safe and has the advantage of making amenable to treatment certain forms of ileocolic and ileo-ileal intussusception which cannot be reduced by means of the enema with pressure and also those forms of intussusception which are secondary to local pathologic conditions or to anatomic abnormalities, such as intestinal intussusception complicating enteroid cysts or diverticula.

Archiv für Kinderheilkunde, Stuttgart

117: 145-224 (July 21) 1939

*Peculiar Disease of Bronchioles in Nurslings (Interstitial Edema Pneumonia). G. Raspe.—p. 145.
Lymphatic Reaction During Childhood. R. Herget.—p. 152.
Evaporated Milk in Feeding of Nurslings. K. Scheer.—p. 180.
Cholepathies During Childhood: Icterus Caused by Mechanical Occlusion in Girl, Aged 2. W. Goeters.—p. 195.
Hypertension in Diphtheria. Inge Fromm.—p. 198.

Peculiar Disease of Bronchioles in Nurslings.—Raspe describes a peculiar pulmonary disorder which was observed in fifteen nurslings. The majority of the nurslings who contracted this disorder were prematurely born or weak and of subnormal weight. Their ages varied between 7 weeks and 3 months. The maternal anamneses revealed nothing abnormal, at any rate no record of diseases during gestation. However, all the nurslings had had an infection of the upper air passages one or several weeks previous to the development of the pulmonary disorder. The clinical aspects of the pulmonary disorder did not differ greatly from those of pneumonia. The onset was rather sudden, with severe dyspnea, tachypnea, ala nasi respiration, pale cyanotic appearance and slight cough. The infants were usually restless, probably as the result of the great air hunger. The spleen and the liver were nearly always palpable. The temperatures were usually subfebrile and examination of the blood generally disclosed anemia. The physical examination of the lung gave but little information, except that the air content of the lungs was reduced, which was indicated by an increased feeling of resistance during direct palpatory percussion. The respiratory sounds were usually surprisingly soft and hollow. Rales were rarely perceptible. Treatment proved ineffective. Death, with the aspects of suffocation, followed after three to six days. In one nursling the intravenous injection of concentrated solution of dextrose had a favorable effect, but the evaluation of this treatment is impossible since a definite diagnosis can be made only during necropsy. Roentgenoscopy disclosed diffuse, cloudy shadows as seen in atelectasis. On the basis of the clinical aspects, the disorder had to be diagnosed as bronchiolitis, pneumonia or mixed forms of these processes. Only the pathologic anatomic aspects indicate that this disorder is a separate clinical entity. Summarizing these aspects, the author says that the process consists in the excretion of an

exudate which is rich in protein and at first is free from cells, into the finest bronchioles, with simultaneous atelectasis of the majority of alveoli. Following this there is shrinkage and epithelization of the edema and accumulation of lymphocytes and plasma cells in the peribronchiolar tissue and in the alveolar septums, possibly as a reaction to the edema. In this stage most of the nurslings died of suffocation, since the main part of the pulmonary parenchyma could no longer function in the exchange of gases. The author thinks that the disorder is of infectious origin, although the bacteriologic tests produced no uniform results. He also considers it possible that allergization plays a part. This pulmonary process has been observed also in other clinics and it is suggested that it might be identical with the "catarrhe suffocant" (suffocating catarrh) described by French authors.

Deutsche medizinische Wochenschrift, Leipzig

65: 1109-1148 (July 14) 1939. Partial Index

Heart and Circulation in Hyperthyroidism: Results of Electrocardiographic Investigations. K. Spang and C. Korth.—p. 1109.
Peptic Ulcer. G. von Bergmann.—p. 1112.
Simmonds's Disease. D. Loos.—p. 1115.
Vitamin C and Carbohydrate Metabolism. Erika Wille.—p. 1117.
Vitamin Character of Nicotinic Acid Amide. T. Morell.—p. 1126.
Biologic Antagonism Between Testosterone Propionate and Estrogen in Animal Experiment. A. G. Peralta Ramos.—p. 1127.
*Hyperostosis Frontalis Interna as Symptom of Hypophysial Diabetes. H. Bartelheimer.—p. 1129.

Hyperostosis Frontalis Interna in Hypophysial Diabetes.—Bartelheimer observed several cases of diabetes in which x-ray examination demonstrated the existence of a hyperostosis frontalis interna. The cases presented hypophysial symptoms that indicated hyperfunction of the anterior lobe of the hypophysis and the author shows that it is justified to assume a close relationship between the internal frontal hyperostosis and hypophysial diabetes. Convinced of the hypophysial origin of the frontal hyperostosis, he emphasizes its diagnostic importance in the differentiation between hyperfunctional diabetes, in which the hypophysis and adrenals are involved, and hypofunctional diabetes, in which the pancreas is involved. Further, he directs attention to the constant occurrence of adiposity in cases of frontal hyperostosis and suggests that this indicates deviations in the activity of the basophil cells. Earlier observations had led him to believe that hyperfunction of the basophil cells of the anterior lobe of the hypophysis is responsible for the development of hypophysial diabetes and he thinks that related hypophysial disturbances are responsible for the concurrence of hyperostosis frontalis and hypophysial diabetes. Regarding the treatment of the intense frontal headaches, which are frequently associated with hyperostosis frontalis interna, he says that in one case he was able to counteract them by means of the administration of estrogenic substance (progynon).

Klinische Wochenschrift, Berlin

18: 917-948 (July 8) 1939. Partial Index

Hepatorenal Syndrome and Hyposthenuria. Nonnenbruch.—p. 917.
Methods of Nonspecific Therapy. W. Weichardt.—p. 920.
C Hypervitaminosis. H. Rietschel.—p. 923.
Effect of Androgen on the Glycogen, Phosphocreatine and Adenylpyrophosphate Content of the Myocardium. H. Schumann.—p. 925.
*Quantitative Determination of Nicotinic Acid and Nicotinic Acid Amide in Urine, Tissues and Blood. K. Ritsert.—p. 934.

Nicotinic Acid Determination in Body Tissues.—Ritsert describes the procedures for and the results of determining the nicotinic acid and the nicotinic acid amide content in the urine, organs and blood of human and animal bodies. His procedures are a modification of the bromcyananiline method and were carried out with the aid of the Pulfrich graduated Zeiss photometer. For the urine test, requiring as little as from 10 to 20 cc. of urine, unselected healthy persons (sex not indicated) were examined. These tests indicated an average nicotinic acid content of from 50 to 300 mg. per hundred cubic centimeters of urine (laboratory tests of the urine of normal rabbits yielded results of between 270 and 650 mg., those of rats from 450 to 650 mg.). To gage the rapidity of excretion, quantities of 100 and 1,000 mg. of nicotinic acid amide were administered, orally and subcutaneously, to rabbits. The major portion of this was eliminated within the first twenty-four hours. Where large doses were administered, only small quantities could be traced: 16 per cent in 100 mg. administration and from 30.6 to 36.9 per cent in 1,000 mg., allowance being made for the normal amount of nicotinic acid in the urine. It is uncertain whether portions of the amide are destroyed within the body or whether its nitrogen undergoes quinquivalent transition, thereby ceasing to be colorimetrically ascertainable. The experiment for nicotinic acid content in the organs and tissues was performed on a rabbit according to the method described by the author. The organs examined were the liver, kidney, heart, brain and spinal cord, lung and muscles and flesh. They furnished the following percentage rates per hundred grams of the organ: liver 7.85 mg., kidney 3.8 mg., heart 3.4 mg., brain and spinal cord 1.2 mg., lung 0.9 mg. and musculature (including the flesh) 6.47 mg. The analysis of the blood for nicotinic acid, according to the author's method, which requires as little as 5 cc. of blood, showed the presence of nicotinic acid or its amide in quantities of from 330 to 460 mg. per hundred cubic centimeters compared with 395 mg. in experimentations on a castrated ram and from 380 to 460 mg. in rabbits. The author emphasizes throughout the necessity of exactness in the application of the method, stressing especially saponification to preserve the amide of the nicotine acid complex. The disadvantage of using the toxic bromcyananiline is more than outweighed by the simplicity of the method and its suitability for serial examinations.

Zeitschrift für Krebsforschung, Berlin

49: 1-136 (June 24) 1939. Partial Index

Epithelioma of Trunk and Extremities. W. Schafft.—p. 1.
Cancer Diagnosis by Means of Polarigraphic Serum Examination. H.-E. Wedemeyer and T. Daur.—p. 10.
Significance of Lipoid Tumors. A. Lang.—p. 20.
Statistical Reports on 2,065 Cases of Malignant Tumors of the Female Genitalia. Vilma Janisch-Raškovič.—p. 29.
Biochemistry of Tumors. Enzyme Systems in Jensen Sarcoma. H. von Euler, G. Günther and N. Forsman.—p. 46.
*Abuse of Tobacco and Carcinoma of the Lungs. F. H. Müller.—p. 57.

Abuse of Tobacco and Carcinoma of Lungs.—Müller states that considerable increase of primary carcinoma of the lungs has been observed in the recent decades. To explain this increase various causes have been pointed out, such as increased street dust, exhaust gases of motor cars, tarring of the streets, war gases, x-rays, trauma, influenza, tuberculosis and increasing industrialization. There appears to be agreement only as to the exogenic character of the causes. Increased attention has been called of late to the significance of smoking as a cause of carcinoma, and the simultaneous increase of carcinoma of the lungs and consumption of tobacco supports this view. The tar content of tobacco is due mainly to the lignified parts of the leaves such as the veins, and these have been used lately in increased quantities in the manufacture of tobacco. The cancerigenic effect of tobacco tar has been demonstrated on experimental animals. Continued use of tobacco creates in man a disposition to cancer at the place of provocation. The time needed for creating this disposition varies for different persons. The author observed lately a relatively large number of patients with carcinoma of the lungs at the municipal hospital in Cologne. Prompted by this observation he carried out a statistical survey on ninety-six dead patients as to smoking habits and other factors acting on the respiratory tracts, such as soot, dust, smoke, tar, vapors, exhaust gases, coal, metal dust and chemicals. Previous diseases of the respiratory tracts were likewise recorded. Of the ninety-six persons, eighty-six were male and showed the following result as to smoking habits: extreme smokers twenty-five (29.07 per cent), very heavy smokers eighteen (20.93 per cent), heavy smokers thirteen (15.12 per cent), moderate smokers twenty-seven (31.39 per cent) and nonsmokers three (3.49 per cent). Comparison between these and eighty-six healthy persons as to daily consumption of tobacco disclosed that the healthy persons smoked considerably less and that most of them were moderate and medium heavy smokers. On the basis of this statistical survey and bearing in mind the positive results obtained in animal experiments, the author concludes that the great increase of tobacco consumption is primarily responsible for the increase of primary carcinoma of the lungs. The fact that about one third of the subjects surveyed smoked moderately or not at all indicates the presence of other cancerigenic factors besides smoking, such as influenza and industrial working conditions. The great significance of the latter can be inferred from various indications but needs further study. Members of families disposed to cancer and persons with chronic catarrhs of the respiratory tracts should be dissuaded from smoking.

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